

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2	"5763221".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 09:49
L2	2	"6146853".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 10:00
L3	57	pf1022\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 10:00
L4	3	(midoh.in. or okakura.in. or miyamoto.in. or watanabe.in. or yanai.in. or yasutake.in. or aihara.in. or futamura.in. or kleinkauf.in. or murakami.in.) and pf1022?	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 10:03
S1	2	chiaii!	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 09:07
S2	1	chitinase and (nepenthes or drosera or dionea or sarracenia)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/13 10:25
S3	2	"20030008370".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/13 16:41
S4	2	"200042203".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 08:13
S5	3	"2001023542".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 08:14
S6	3	"2001023542"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 08:34
S7	11	"9700944"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 08:37

EAST Search History

S8	2	"5763221".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/15 09:26
S9	38	pf1022	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 09:29
S10	13062	Haese.in. or Schubert.in. or herrmann.in. or Zocher.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 09:30
S11	11	(Haese.in. or Schubert.in. or herrmann.in. or Zocher.in.) and (N-methyldepsipeptide or Fusarium)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 09:33
S12	1	"0578616".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 09:34
S13	3	"0578616"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 09:34
S14	3	"0578616"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 09:34
S15	0	EP0578616	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 09:34
S16	3925037	EP "0578616"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 09:35
S17	2	"5827706".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 09:37
S18	4	leitner.in. and cyclosporin	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/14 09:37
S19	1	(midoh.in. or okakura.in. or miyamoto.in. or watanabe.in. or yanai.in. or yasutake.in. or aihara.in. or futamura.in. or kleinkauf.in. or murakami.in.) and pf1022?	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2004/01/15 09:28

EAST Search History

S20	0	(depsipeptide adj (synthase or synthetase)) near5 (mutation or mutagenesis)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/01/12 12:34
S21	0	(depsipeptide adj (synthase or synthetase)) near10 (mutation or mutagenesis)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/01/12 12:34
S22	2	(depsipeptide adj (synthase or synthetase))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/01/12 12:39
S23	13	cyclosporin adj synthetase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/01/12 12:39
S24	9	S23 and (mutation or mutagenesis)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/01/12 12:40
S25	21388	FERM BP-2671	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/11/28 07:00
S26	20	FERM adj BP-2671	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/11/28 07:03
S27	32	pf adj "1022"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/11/28 07:03
S28	9	S27 and extract	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/11/28 07:03
S29	3	"6916641".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 09:08
S30	3	"7109018".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 09:14
S31	2	"5116815".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 09:29

EAST Search History

S33	3	"2002077244".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 09:33
S34	2	"20020077244".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 09:33
S35	1	"200277244".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 09:37



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- Select PubMed under the Links menu to retrieve all records for the MeSH Term.
- Select [NLM MeSH Browser](#) under the Links menu for additional information.

1: PFSYN depsipeptide synthetase [Substance Name]

involved in biosynthesis of PF1022A; isolated from Mycelia sterilia
Date introduced: July 17, 2000

Registry Number: EC 6.3.2.-

Heading Mapped to:

- [Peptide Synthases](#)

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Dec 13 2006 10:56:50

No
V.S.
Class
place
in 435/183

Search Results for 10/070387_20061214

FILE 'REGISTRY' ENTERED AT 08:30:06 ON 14 DEC 2006
E "PF1022"/CN 25

L3 2 S E4 OR E5

FILE 'CPLUS' ENTERED AT 08:30:46 ON 14 DEC 2006

E MIDOH NAOKI/AU 25

L4 3 S (E2 OR E3) AND (L1 OR PFSYN OR PF1022?)
E OKAKURA KAORU/AU 25

L5 3 S (E1 OR E2 OR E3) AND (L1 OR PFSYN OR PF1022?)
E MIYAMOTO KOICHI/AU 25
E MIYAMOTO K/AU 25

L6 4 S (E3 OR E146 OR E147 OR E148) AND (L1 OR PFSYN OR PF1022?)
E WATANABE M/AU 25

L7 6 S (E3 OR E41) AND (L1 OR PFSYN OR PF1022?)
E YANAI K/AU 25

L8 0 S (E3) AND (L1 OR PFSYN OR PF1022?)
E YANAI KOJI/AU 25

L9 6 S (E1 OR E2 OR E3) AND (L1 OR PFSYN OR PF1022?)
E YASUTAKE T/AU 25

L10 1 S (E3 OR E14) AND (L1 OR PFSYN OR PF1022?)
E AIHARA S/AU 25

L11 1 S (E3 OR E7 OR E8) AND (L1 OR PFSYN OR PF1022?)
E FUTAMURA T/AU 25

L12 1 S (E3 OR E5) AND (L1 OR PFSYN OR PF1022?)
E KLEINKAUF H/AU 25

L13 3 S (E3 OR E4) AND (L1 OR PFSYN OR PF1022?)
E MURAKAMI T/AU 25

L14 7 S (E3 OR E89 OR E90) AND (L1 OR PFSYN OR PF1022?)

L15 9 S L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 O

L16 9 DUP REM L15 (0 DUPLICATES REMOVED)

FILE 'MEDLINE, AGRICOLA, CPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT
08:40:55 ON 14 DEC 2006

L17 17.0 S L1 OR PFSYN OR PF1022?

L18 32 S L17 AND MYCELIA

L19 6 S L18 AND ((CELL? (3A) EXTRACT) OR (CELL? (3A) SYNTHESIS) OR (C
L20 3 DUP REM L19 (3 DUPLICATES REMOVED)

L21 26 S L18 NOT L19

L22 1 S L17 AND AGONOMYCETES

L23 14 S L17 AND AGONOMYCETALES

L24 8 S L23 NOT (L22 OR L18)

L25 6 DUP REM L24 (2 DUPLICATES REMOVED)

L26 32 S L17 AND (POLYPEPTIDE OR PROTEIN OR SYNTHETASE OR SYNTHASE)

L27 13 S L26 NOT (L23 OR L22 OR L18)

L28 8 DUP REM L27 (5 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 09:56:01 ON 14 DEC 2006

Search Results for 10/070387_20061214

L21 ANSWER 1 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2005551700 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16228266
TITLE: Influence of the cyclooctadepsipeptides PF1022A and PF1022E as natural products on the design of semi-synthetic anthelmintics such as emodepside.
AUTHOR: Jeschke R; Iinuma K; Harder A; Schindler M; Murakami T
CORPORATE SOURCE: Bayer CropScience AG, Research and Development, Chemistry Insecticides, Alfred-Nobel-Strasse 50, 40789, Monheim am Rhein, Germany,. peter.jeschke@bayercropscience.com
SOURCE: Parasitology research, (2005 Oct) Vol. 97 Suppl 1, pp. S11-6.
PUB. COUNTRY: Journal code: 8703571. ISSN: 0932-0113. Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 18 Oct 2005
Last Updated on STN: 13 Dec 2006
AB The 24-membered cyclooctadepsipeptide (CODP) PF1022A, the active metabolite of the fungus *imperfectus* *Mycelia sterilia* (*Rosellinia* sp.) isolated from the plant *Camellia japonica* in Japan, is described as a powerful broad-spectrum anthelmintic natural product with low toxicity in animals. Further CODPs such as PF1022B, C, D and E have been isolated from the same culture and their structures have been established. Both PF1022A and PF1022E serve as valuable starting materials for the synthesis of semi-synthetic CODP derivatives with improved intrinsic anthelmintic potency and broad-spectrum activity. It was found that in most cases the di-substituted PF1022A derivatives showed a greater (or equal) activity by oral application against the gastrointestinal nematode *Haemonchus contortus* compared to the corresponding mono-substituted PF1022A analogues as exemplified by emodepside. In order to get additional information on the bioactive conformation, emodepside was transformed into its mono- and tetra-thionated derivatives by isosteric replacement. In the light of the increased efficacy of these derivatives against *H. contortus* or *Trichostrongylus colubriformis*, it has been suggested that the asymmetric conformation clearly influences the anthelmintic activity of CODPs. Although useful synthetic pathways are available today for the preparation of the semi-synthetic CODP emodepside, the fermentative production of its bis-para-nitro and bis-para-amino precursors could be the process used for its industrial-scale production in the future.

L21 ANSWER 2 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2005551697 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16228263
TITLE: Mechanisms of action of emodepside.
AUTHOR: Harder A; Holden-Dye L; Walker R; Wunderlich F
CORPORATE SOURCE: Bayer HealthCare AG, Animal Health Division, Research and Development, Parasiticides, 51368, Leverkusen, Germany,. achim.harder@bayerhealthcare.com
SOURCE: Parasitology research, (2005 Oct) Vol. 97 Suppl 1, pp. S1-S10.
PUB. COUNTRY: Journal code: 8703571. ISSN: 0932-0113. Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals

Search Results for 10/070387_20061214

ENTRY DATE: Entered STN: 18 Oct 2005

Last Updated on STN: 13 Dec 2006

AB The research of the class of cyclic octadepsipeptides started at the beginning of the 1990s. PF1022A, the starting material of emodepside, is a natural secondary metabolite of the fungus *Mycelia sterilia*, which belongs to the microflora of the leaves of *Camellia japonica*. PF1022A consists of four N-methyl-L:-leucins, two D:-Iactic acids and two D:-phenyllactic acids, which build up a cyclic octadepsipeptide with an alternating L:-D:-L:-D:-L:-configuration. Emodepside is a semisynthetic derivative of PF1022A, which contains a morpholine attached in para position at each of both D:-phenyllactic acids. Emodepside is efficacious against a variety of gastrointestinal nematodes. Emodepside binds to a presynaptic latrophilin receptor in nematodes. The following presynaptic signal transduction occurs via activation of Gqalpha protein and phospholipase-Cbeta, which leads to mobilization of diacylglycerol (DAG). DAG then activates UNC-13 and synaptobrevin, two proteins which play an important role in presynaptic vesicle-functioning. This finally leads to the release of a currently unidentified transmitter. The transmitter (or modulator) exerts its effects at the postsynaptic membrane and induces a flaccid paralysis of the pharynx and the somatic musculature in nematodes.

L21 ANSWER 3 OF 26 MEDLINE on STN

ACCESSION NUMBER: 2003438302 MEDLINE

DOCUMENT NUMBER: PubMed ID: 13678839

TITLE: Cyclooctadepsipeptides--an anthelmintically active class of compounds exhibiting a novel mode of action..

AUTHOR: Harder Achim; Schmitt-Wrede Hans-Peter; Krucken Jurgen; Marinovski Predrag; Wunderlich Frank; Willson James; Amliwala Kiran; Holden-Dye Lindy; Walker Robert

CORPORATE SOURCE: Bayer AG, BHC, AH-RD-Para, Alfred-Nobel-Strasse 50, D-40789 Manheim, Germany.. achim-harder-ah@bayer.ag.de

SOURCE: International journal of antimicrobial agents, (2003 Sep) Vol. 22, No. 3, pp. 318-31. Ref: 52
Journal code: 9111860. ISSN: 0924-8579.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200401

ENTRY DATE: Entered STN: 23 Sep 2003

Last Updated on STN: 21 Jan 2004

Entered Medline: 20 Jan 2004

AB There are three major classes of anthelmintics for veterinary use: the benzimidazoles/prebenzimidazoles, the tetrahydropyrimidines/imidazothiazoles, and the macrocyclic lactones. In nematodes, there are five targets for the existing anthelmintics: the nicotinic acetylcholine receptor which is the target of tetrahydropyrimidines/imidazothiazoles and indirectly that of the acetylcholinesterase inhibitors; the GABA receptor which is the target of piperazine, the glutamate-gated chloride channel as the target of the macrocyclic lactones, and beta-tubulin as the target of prebenzimidazoles/benzimidazoles. All these anthelmintics are now in serious danger because of the worldwide spread of resistant nematodes in sheep, cattle, horses and pigs. The class of cyclooctadepsipeptides has entered the scene of anthelmintic research in the early 1990s.

PF1022A, the first anthelmintically active member, is a natural compound from the fungus *Mycelia sterilia* that belongs to the microflora of the leaves of the *Camellia japonica*. PF1022A contains 4 N-Methyl-L-leucines, 2 D-lactic acids and 2-D-phenyllactic acids arranged as a cyclic octadepsipeptide with an alternating L-D-L-configuration. Emodepside is a semisynthetic derivative of

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PF1022A with a morpholine ring at each of the two D-phenyllactic acids in para position. The anthelmintic activity is directed against gastrointestinal nematodes in chicken, mice, rats, meriones, dogs, cats, sheep, cattle and horses. Moreover, emodepside is active against *Trichinella spiralis* larvae in muscles, microfilariae and preadult filariae and *Dictyocaulus viviparus*. PF1022A and emodepside are fully effective against benzimidazole-, levamisole or ivermectin-resistant nematodes in sheep and cattle. In *Ascaris suum* both cyclooctadepsipeptides lead to paralysis indicating a neuropharmacological action of these compounds. Using a PF1022A-ligand immunoscreening of a cDNA library from *Haemonchus contortus* a cDNA clone of 3569 base pairs could be identified. This clone codes for a novel 110 kDa heptahelical transmembrane receptor, named HC110R. Database- and phylogenetic analysis reveals that this receptor is a homolog to B0457.1 from *Caenorhabditis elegans* and has significant similarity to latrophilins from human, cattle and rat. HC110R is located in the plasma membrane and in lysosomes and endosomes. Alpha-latrotoxin, the poison of the black widow spider, binds at a 54 kDa aminoterminal fragment of HC110R. After binding a Ca²⁺-influx into HEK293 cells is induced which can be blocked by EGTA, Cd²⁺ or nifedipine. PF1022A or emodepside also bind to this 54 kDa aminoterminal region of HC110R and interact with the functional responses of alpha-latrotoxin. In *C. elegans* antibodies against the C-or N-terminus of HC110R bind to the B0457.1 protein located in the pharynx. Electrophysiological studies reveal that emodepside inhibits pharyngeal pumping of the nematodes in a concentration dependent way with an IC(50) value of about 4 nM. Thus, it is tempting to speculate that emodepside exerts its action on nematodes via a latrophilin-like receptor which might have an important regulatory function on pharyngeal pumping.

L21 ANSWER 4 OF 26 MEDLINE on STN
ACCESSION NUMBER: 92324946 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1624372
TITLE: A new anthelmintic cyclodepsipeptide, PF1022A.
AUTHOR: Sasaki T; Takagi M; Yaguchi T; Miyadoh S; Okada T; Koyama M
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Meiji Seika Kaisha Ltd., Yokohama, Japan.
SOURCE: The Journal of antibiotics, (1992 May) Vol. 45, No. 5, pp. 692-7.

PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 21 Aug 1992
Last Updated on STN: 29 Jan 1999
Entered Medline: 13 Aug 1992

AB The novel anthelmintic cyclodepsipeptide PF1022A was isolated from cultured mycelia of *Mycelia Sterilia* PF1022 (FERM BP-2671). It showed strong anthelmintic activities against *Ascaridia galli* in chickens. The structure of PF1022A was determined to be cyclo(D-lactyl-L-N-methylleucyl-D-3-phenyllactyl-L-N-methyleucyl-D-lactyl-L-N-methyleucyl-D-3-phenyllactyl-L-N-methyleucyl) by spectroscopic analyses and chemical studies.

L21 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:729020 CAPLUS
DOCUMENT NUMBER: 140:174164
TITLE: Cyclooctadepsipeptides-an anthelmintically active class of compounds exhibiting a novel mode of action
AUTHOR(S): Harder, Achim; Schmitt-Wrede, Hans-Peter; Krucken,

Jurgen; Marinovski, Predrag; Wunderlich, Frank;
Willson, James; Amliwala, Kiran; Holden-Dye, Lindy;
Walker, Robert
CORPORATE SOURCE: AH-RD-Para, BHC, Bayer AG, Manheim, D-40789, Germany
SOURCE:

International Journal of Antimicrobial Agents (2003),
22 (3), 318-331

CODEN: IAAGEA; ISSN: 0924-8579

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. There are 3 major classes of anthelmintics for veterinary use: the benzimidazoles/prebenzimidazoles, the tetrahydropyrimidines/imidazothiazoles, and the macrocyclic lactones. In nematodes, there are 5 targets for the existing anthelmintics: the nicotinergic acetylcholine receptor which is the target of tetrahydropyrimidines/imidazothiazoles and indirectly that of the acetylcholinesterase inhibitors; the GABA receptor which is the target of piperazine, the glutamate-gated chloride channel as the target of the macrocyclic lactones, and ss-tubulin as the target of prebenzimidazoles/benzimidazoles. All these anthelmintics are now in serious danger because of the worldwide spread of resistant nematodes in sheep, cattle, horses and pigs. The class of cyclooctadepsipeptides has entered the scene of anthelmintic research in the early 1990s.

PF1022A, the first anthelmintically active member, is a natural compound from the fungus *Mycelia sterilia* that belongs to the microflora of the leaves of the *Camellia japonica*. PF1022A contains 4 N-Methyl-l-leucines, 2 d-lactic acids and 2-d-phenyllactic acids arranged as a cyclic octadepsipeptide with an alternating 1-d-1-configuration. Emodepside is a semisynthetic derivative of PF1022A with a morpholine ring at each of the 2 d-phenyllactic acids in para position. The anthelmintic activity is directed against gastrointestinal nematodes in chicken, mice, rats, meriones, dogs, cats, sheep, cattle and horses. Moreover, emodepside is active against *Trichinella spiralis* larvae in muscles, microfilariae and preadult filariae and *Dictyocaulus viviparus*. PF1022A and emodepside are fully effective against benzimidazole-, levamisole or ivermectin-resistant nematodes in sheep and cattle. In *Ascaris suum* both cyclooctadepsipeptides lead to paralysis indicating a neuropharmacol. action of these compds. Using a PF1022A-ligand immunoscreening of a cDNA library from *Haemonchus contortus* a cDNA clone of 3569 base pairs could be identified. This clone codes for a novel 110 kDa heptahelical transmembrane receptor, named HC110R. Database- and phylogenetic anal. reveals that this receptor is a homolog to B0457.1 from *Caenorhabditis elegans* and has significant similarity to latrophilins from human, cattle and rat. HC110R is located in the plasma membrane and in lysosomes and endosomes. α -Latrotoxin, the poison of the black widow spider, binds at a 54 kDa aminoterminal fragment of HC110R. After binding a Ca²⁺-influx into HEK293 cells is induced which can be blocked by EGTA, Cd²⁺ or nifedipine. PF1022A or emodepside also bind to this 54 kDa aminoterminal region of HC110R and interact with the functional responses of α -latrotoxin. In *C. elegans* antibodies against the C-or N-terminus of HC110R bind to the B0457.1 protein located in the pharynx. Electrophysiol. studies reveal that emodepside inhibits pharyngeal pumping of the nematodes in a concentration dependent way with an

IC50

value of about 4 nM. Thus, it is tempting to speculate that emodepside exerts its action on nematodes via a latrophilin-like receptor which might have an important regulatory function on pharyngeal pumping.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Search Results for 10/070387_20061214

DOCUMENT NUMBER: 137:274081
 TITLE: Biosynthetic production of PF1022 derivatives using p-aminophenyl pyruvate biosynthesis pathway enzymes
 INVENTOR(S): Yanai, Koji; Sumida, Naomi; Watanabe, Manabu; Moriya, Tatsuki; Murakami, Takeshi
 PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
 SOURCE: PCT Int. Appl., 116 pp.
 CODEN: PIIXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002077244	A1	20021003	WO 2002-JP2782	20020322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2441346	AA	20021003	CA 2002-2441346	20020322
EP 1380649	A1	20040114	EP 2002-707130	20020322
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CN 1509334	A	20040630	CN 2002-810040	20020322
NZ 528268	A	20050527	NZ 2002-528268	20020322
NO 2003004072	A	20031119	NO 2003-4072	20030915
US 2004214274	A1	20041028	US 2003-472587	20030922
PRIORITY APPLN. INFO.:			JP 2001-82227	A 20010322
			WO 2002-JP2782	W 20020322

AB A direct fermentation method for biosynthetic production of PF1022 derivs. (in particular, PF1022-220 and PF1022-260) by transformation of PF1022-producing microorganism with genes coding for enzymes involved in the biosynthesis of p-aminophenyl pyruvate from chorismic acid, is provided. Phenylalanine-dependent microorganisms, *Mycelia sterilia* FERM BP-2671, in particular, lacking the endogenous chorismate mutase and/or prephenate dehydrogenase activities, are transformed. *Streptomyces venezuelae* genes papA, papB, and papC, coding for 4-amino-4-deoxychorismate synthase, 4-amino-4-deoxychorismate mutase, and 4-amino-4-deoxyprephenate dehydrogenase, resp., were cloned and used to transform *Mycelia sterilia* FERM BP-2671, whose endogenous chorismate mutase and/or prephenate dehydrogenase activities destroyed via homologous recombination. Production of PF1022-220 and PF1022-260, in *Mycelia sterilia*, transformed with papA, papB, and papC genes, was observed

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:291564 CAPLUS
 DOCUMENT NUMBER: 137:32089
 TITLE: Use of network analysis of metabolic systems in bioengineering
 AUTHOR(S): Schuster, S.; Klamt, S.; Weckwerth, W.; Moldenhauer, F.; Pfeiffer, T.
 CORPORATE SOURCE: Department of Bioinformatics, Max Delbrueck Centre for

Search Results for 10/070387_20061214

SOURCE: Molecular Medicine, Berlin, 13092, Germany
 Bioprocess and Biosystems Engineering (2002), 24(6),
 363-372

PUBLISHER: CODEN: BBEIBV; ISSN: 1615-7591
 Springer-Verlag
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review. Basic ideas and recent developments in network anal. of metabolic systems and various applications of this anal. in bioengineering are reviewed. Central concepts are the null-space to the stoichiometry matrix and the elementary flux modes. The applicability of elementary-modes anal. in biotechnol. is illustrated by the synthesis of the cyclooctadepsipeptides PF1022 in the fungus Mycelia sterilia. Network anal. is also useful in metabolic flux anal. In particular, a procedure for finding out which reaction rates can be uniquely calculated in underdetd. reaction networks is outlined. The concept of 'enzyme subsets' is explained and its use for analyzing genetic regulation is demonstrated. In particular, the correlation between expression data concerning the diauxic shift in yeast and the enzyme subsets in yeast metabolism is discussed.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:798412 CAPLUS

DOCUMENT NUMBER: 135:340830

TITLE: Mycelia sterilia (R)-2-hydroxy-3-phenylpropionate (D-phenyllactate) dehydrogenase and cDNA

INVENTOR(S): Miyamoto, Koichi; Sumida, Naomi; Midoh, Naoki; Murakami, Takeshi; Zocher, Rainer; Kleinkauf, Horst

PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081563	A1	20011101	WO 2001-JP3645	20010426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2407059	AA	20011101	CA 2001-2407059	20010426
AU 2001052608	A5	20011107	AU 2001-52608	20010426
EP 1291417	A1	20030312	EP 2001-925976	20010426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 522584	A	20040227	NZ 2001-522584	20010426
NO 2002005126	A	20021220	NO 2002-5126	20021025
US 2003186410	A1	20031002	US 2002-258472	20021107
US 6916641	B2	20050712		
PRIORITY APPLN. INFO.:			JP 2000-125449	A 20000426
			WO 2001-JP3645	W 20010426

Search Results for 10/070387_20061214

AB A D-phenyllactate dehydrogenase (D-PLDH) of *Mycelia sterilia*, gene, recombinant expression, and use in enzymic synthesis of D-phenyllactate, PF1022, or their derivs., are disclosed. Cloning of D-PLDH cDNA from *Mycelia sterilia* FERM BP-2671 and recombinant expression in *E. coli*, are described. Production of D-phenyllactate from Ph pyruvate was demonstrated. Pyruvate was also used as a substrate, though the activity was only 10% of that with Ph pyruvate as substrate.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:247475 CAPLUS

DOCUMENT NUMBER: 134:277400

TITLE: *Streptomyces venezuelae* genes papA, papB, and papC, coding for 4-amino-4-deoxychorismate synthase, 4-amino-4-deoxychorismate mutase, and 4-amino-4-deoxyprehenate dehydrogenase, recombinant expression, and use in biosynthesis of para-amino or nitro substituted benzene ring-containing compound

INVENTOR(S): Yanai, Koji; Okakura, Kaoru; Yasuda, Shohei; Watanabe, Manabu; Miyamoto, Koichi; Midoh, Naoki; Murakami, Takeshi

PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan

SOURCE: PCT Int. Appl., 83 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023542	A1	20010405	WO 2000-JP6783	20000929
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2386255	AA	20010405	CA 2000-2386255	20000929
AU 2000074496	A5	20010430	AU 2000-74496	20000929
AU 783603	B2	20051110		
EP 1223215	A1	20020717	EP 2000-962989	20000929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NZ 518551	A	20030926	NZ 2000-518551	20000929
US 7109018	B1	20060919	US 2002-89514	20020329
NO 2002001549	A	20020527	NO 2002-1549	20020402
PRIORITY APPLN. INFO.:			JP 1999-276314	A 19990929
			WO 2000-JP6783	W 20000929

AB Microorganisms genetically engineered to produce a secondary metabolite wherein a benzene ring substituted at the para-position with a nitrogen-containing functional group, nitro or amino group, in particular, are disclosed. A microorganism, *Streptomyces*, *Nocardia*, or *Corynebacteria*, in particular, which produces a secondary metabolite having a benzene ring skeleton free from substitution at the para-position by a nitrogen-containing functional group, are transformed with genes participating in the biosynthesis of p-aminophenylpyruvic acid from chorismic acid so as to

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enable the production of a secondary metabolite having a benzene ring skeleton substituted at the para-position by a nitrogen-containing functional group. Biosynthesis of Ph pyruvic acid, p-hydroxyphenyl lactate, phenylalanine, tyrosine, or Ph lactate in those microorganisms are claimed. Biosynthesis of peptides and cyclic depsipeptides, in particular PF1022 derivs., are also claimed. Also, novel genes participating in the biosynthesis of p-aminophenylpyruvic acid from chorismic acid are provided. Streptomyces venezuelae genes papA, papB, and papC, coding for 4-amino-4-deoxychorismate synthase, 4-amino-4-deoxychorismate mutase, and 4-amino-4-deoxyprephenate dehydrogenase, resp., are claimed. Synthesis of 4-amino-4-deoxychorismate was detected in E. coli transformed with papA gene. Reduction in the amount of 4-amino-4-deoxychorismate and increase in the amount of 4-Amino-4-deoxyprephenate was observed in E. coli transformed with papB gene. Reduction in the amount of 4-amino-4-deoxychorismate and 4-amino-4-deoxyprephenate and increase in the amount of p-phenylalanine, the product of aminotransferase reaction on p-aminophenyl pyruvate, was observed in E. coli transformed with papC gene. Production of PF1022-268, cyclo[MeLeu-Lac-MeLeu-(O2N)PhLac-MeLeu-Lac-MeLeu-PhLac], PF1022-269, and cyclo[MeLeu-Lac-MeLeu-(H2N)PhLac-MeLeu-Lac-MeLeu-PhLac] in Mycelia sterilia, transformed with papA, papB, and papC genes, was observed

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:185930 CAPLUS
 DOCUMENT NUMBER: 134:218008
 TITLE: DNA sequence of the promoter and the terminator of Abp1 gene of Mycelia sterilia and the its regulation for transcription
 INVENTOR(S): Watanabe, Manabu; Murakami, Takeshi
 PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
 SOURCE: PCT Int. Appl., 26 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018219	A1	20010315	WO 2000-JP6104	20000907
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2384000	AA	20010315	CA 2000-2384000	20000907
AU 2000068742	A5	20010410	AU 2000-68742	20000907
AU 782525	B2	20050804		
EP 1221489	A1	20020710	EP 2000-957010	20000907
EP 1221489	B1	20061129		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NZ 517463	A	20031031	NZ 2000-517463	20000907
US 6913905	B1	20050705	US 2002-70386	20000907
NO 2002000941	A	20020506	NO 2002-941	20020227
PRIORITY APPLN. INFO.:			JP 1999-252851	A 19990907

WO 2000-JP6104 W 20000907

AB This invention provides an endogenous gene promoter in filamentous fungi (*Mycelia sterilia*) which has high transcription efficiency. A highly expressed gene (Abp1) was isolated from *Mycelia sterilia* (PF 1022) by randomly sequencing the clones in cDNA library and its genomic DNA was also isolated which containing promoter and terminator region. The reporter gene was highly expressed under Abp1 gene promoter when transformed into *Mycelia sterilia* (PF1022).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:462356 CAPLUS

DOCUMENT NUMBER: 117:62356

TITLE: A new anthelmintic cyclodepsipeptide, PF1022A

AUTHOR(S): Sasaki, Toru; Takagi, Masayuki; Yaguchi, Takashi;

Miyadoh, Shinji; Okada, Tadaaki; Koyama, Masao

CORPORATE SOURCE: Pharm. Res. Lab., Meiji Seika Kaisha Ltd., Yokohama, 222, Japan

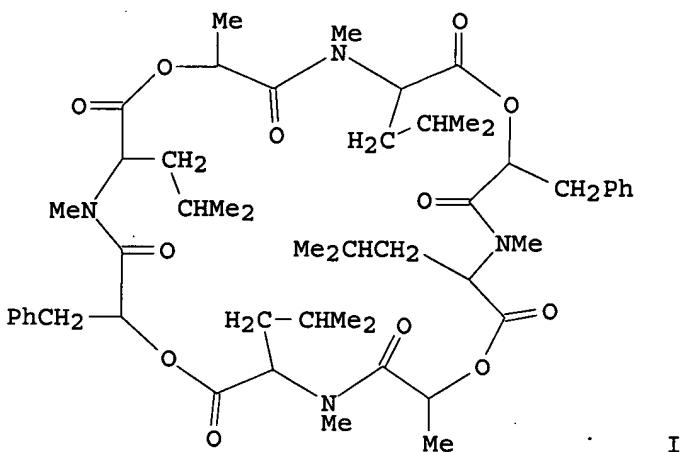
SOURCE: Journal of Antibiotics (1992), 45(5), 692-7

CODEN: JANTAJ; ISSN: 0021-8820

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB The novel anthelmintic cyclodepsipeptide PF1022A was isolated from cultured mycelia of *Mycelia Sterilia* PF1022 (FERM BP-2671). It showed strong anthelmintic activities against *Ascaridia galli* in chickens. The structure of PF1022A was determined to be cyclo(D-lactyl-L-N-methylleucyl-D-3-phenyllactyl-L-N-methylleucyl-D-lactyl-L-N-methylleucyl-D-3-phenyllactyl-L-N-methyleucyl, I) by spectroscopic analyses and chemical studies.

L21 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:183852 CAPLUS

DOCUMENT NUMBER: 114:183852

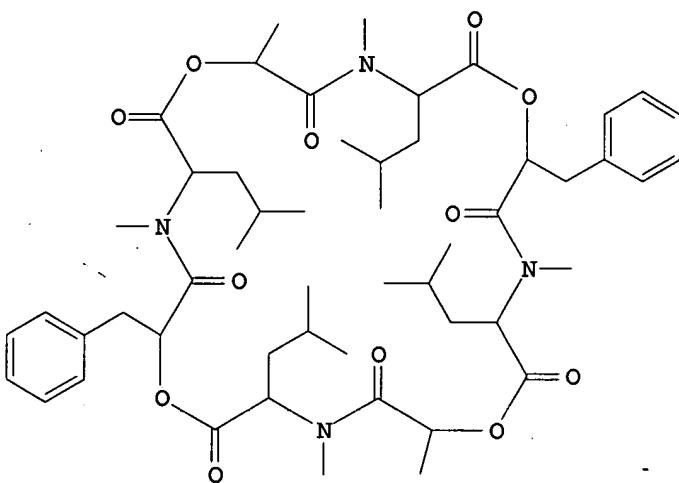
TITLE: Anthelmintic PF 1022 manufactured with an Agonomycete (*mycelia sterilia*)

INVENTOR(S): Takagi, Masayuki; Okada, Tadaaki; Akai, Naotoshi; Yaguchi, Takashi; Miyadoh, Shinji; Shomura, Takashi; Sasaki, Toru; Sezaki, Masaji; Shimizu, Takao; Niida, Masashi

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PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
 SOURCE: Eur. Pat. Appl., 20 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 382173	A2	19900816	EP 1990-102328	19900206
EP 382173	A3	19910605		
EP 382173	B1	19951206		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE NO 9000528	A	19900808	NO 1990-528	19900205
NO 176766	B	19950213		
NO 176766	C	19950524		
JP 03035796	A2	19910215	JP 1990-25176	19900206
US 5116815	A	19920526	US 1990-475544	19900206
AT 131161	E	19951215	AT 1990-102328	19900206
ES 2083392	T3	19960416	ES 1990-102328	19900206
CA 2009508	AA	19900807	CA 1990-2009508	19900207
CA 2009508	C	20010703		
AU 9049215	A1	19900816	AU 1990-49215	19900207
AU 620689	B2	19920220		
CN 1046940	A	19901114	CN 1990-101176	19900207
CN 1027288	B	19950104		
KR 132051	B1	19980411	KR 1990-1460	19900207
PRIORITY APPLN. INFO.:			JP 1989-26739	A 19890207
GI				



- AB Anthelmintic PF 1022 (I) that is useful for treatment or prevention of parasitic infection of animals is manufactured with an Agonomycete (*Mycelia sterilia*). Agonomycete PF 1022 was cultured in 35 L medium containing starch syrup, soybean oil, wheat germ, soybean cake, yeast, and salts for 5 days at 26° with aeration and stirring. I 24.9 mg was recovered from the culture filtrate after extraction with acetone and Et acetate and chromatog. Anthelmintic activity of I in a variety of animals, e.g., chickens artificially infected with roundworms (*Ascaridia galli*), was demonstrated.

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L21 ANSWER 13 OF 26 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:48568 BIOSIS
DOCUMENT NUMBER: PREV200400050701
TITLE: Cyclooctadepsipeptides: An anthelmintically active class of compounds exhibiting a novel mode of action.
AUTHOR(S): Harder, Achim [Reprint Author]; Schmitt-Wrede, Hans-Peter; Kruecken, Juergen; Marinovski, Predrag; Wunderlich, Frank; Willson, James; Amliwala, Kiran; Holden-Dye, Lindy; Walker, Robert
CORPORATE SOURCE: AH-RD-Para, Bayer AG, BHC, Alfred-Nobel-Str. 50, D-40789, Manheim, Germany
achim.harder.ah@bayer-ag.de
SOURCE: International Journal of Antimicrobial Agents, (September 2003) Vol. 22, No. 3, pp. 318-331. print.
ISSN: 0924-8579.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Jan 2004
Last Updated on STN: 21 Jan 2004

AB There are three major classes of anthelmintics for veterinary use: the benzimidazoles/prebenzimidazoles, the tetrahydropyrimidines/imidazothiazoles, and the macrocyclic lactones. In nematodes, there are five targets for the existing anthelmintics: the nicotinic acetylcholine receptor which is the target of tetrahydropyrimidines/imidazothiazoles and indirectly that of the acetylcholinesterase inhibitors; the GABA receptor which is the target of piperazine, the glutamate-gated chloride channel as the target of the macrocyclic lactones, and beta-tubulin as the target of prebenzimidazoles/benzimidazoles. All these anthelmintics are now in serious danger because of the worldwide spread of resistant nematodes in sheep, cattle, horses and pigs. The class of cyclooctadepsipeptides has entered the scene of anthelmintic research in the early 1990s.

PF1022A, the first anthelmintically active member, is a natural compound from the fungus *Mycelia sterilia* that belongs to the microflora of the leaves of the *Camellia japonica*. PF1022A contains 4 N-Methyl-L-leucines, 2 D-lactic acids and 2-D-phenyllactic acids arranged as a cyclic octadepsipeptide with an alternating L-D-L-configuration. Emodepside is a semisynthetic derivative of PF1022A with a morpholine ring at each of the two D-phenyllactic acids in para position. The anthelmintic activity is directed against gastrointestinal nematodes in chicken, mice, rats, meriones, dogs, cats, sheep, cattle and horses. Moreover, emodepside is active against *Trichinella spiralis* larvae in muscles, microfilariae and preadult filariae and *Dictyocaulus viviparus*. PF1022A and emodepside are fully effective against benzimidazole-, levamisole or ivermectin-resistant nematodes in sheep and cattle. In *Ascaris suum* both cyclooctadepsipeptides lead to paralysis indicating a neuropharmacological action of these compounds. Using a PF1022A-ligand immunoscreening of a cDNA library from *Haemonchus contortus* a cDNA clone of 3569 base pairs could be identified. This clone codes for a novel 110 kDa heptahelical transmembrane receptor, named HC110R. Database and phylogenetic analysis reveals that this receptor is a homolog to B0457.1 from *Caenorhabditis elegans* and has significant similarity to latrophilins from human, cattle and rat. HC110R is located in the plasma membrane and in lysosomes and endosomes. alpha-Latrotoxin, the poison of the black widow spider, binds at a 54 kDa aminoterminal fragment of HC110R. After binding a Ca²⁺-influx into HEK293 cells is induced which can be blocked by EGTA, Cd²⁺ or nifedipine. PF1022A or emodepside also bind to this 54 kDa aminoterminal region of HC110R and interact with the functional responses of alpha-latrotoxin. In *C. elegans* antibodies against the C-or N-terminus of HC110R bind to the B0457.1 protein located in the pharynx. Electrophysiological studies reveal that emodepside

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inhibits pharyngeal pumping of the nematodes in a concentration dependent way with an IC₅₀ value of about 4 nM. Thus, it is tempting to speculate that emodepside exerts its action on nematodes via a latrophilin-like receptor which might have an important regulatory function on pharyngeal pumping.

L21 ANSWER 14 OF 26 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:371640 BIOSIS

DOCUMENT NUMBER: PREV200200371640

TITLE: Use of network analysis of metabolic systems in bioengineering.

AUTHOR(S): Schuster, S. [Reprint author]; Klamt, S.; Weckwerth, W.; Moldenhauer, F.; Pfeiffer, T.

CORPORATE SOURCE: Department of Bioinformatics, Max Delbrueck Centre for Molecular Medicine, 13092, Berlin-Buch, Germany
stschust@mdc-berlin.de

SOURCE: Bioprocess and Biosystems Engineering, (March, 2002) Vol. 24, No. 6, pp. 363-372. print.

ISSN: 1615-7591.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 3 Jul 2002

Last Updated on STN: 3 Jul 2002

AB Basic ideas and recent developments in network analysis of metabolic systems and various applications of this analysis in bioengineering are reviewed. Central concepts are the null-space to the stoichiometry matrix and the elementary flux modes. The applicability of elementary-modes analysis in biotechnology is illustrated by the synthesis of the cyclooctadepsipeptides PF1022 in the fungus Mycelia sterilia. Network analysis is also useful in metabolic flux analysis. In particular, a procedure for finding out which reaction rates can be uniquely calculated in underdetermined reaction networks is outlined. The concept of 'enzyme subsets' is explained and its use for analysing genetic regulation is demonstrated. In particular, the correlation between expression data concerning the diauxic shift in yeast and the enzyme subsets in yeast metabolism is discussed.

L21 ANSWER 15 OF 26 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1996:17710 BIOSIS

DOCUMENT NUMBER: PREV199698589845

TITLE: Effects of PF1022A on Nippostrongylus brasiliensis in rats and Hymenolepis nana in mice.

AUTHOR(S): Wang, Ming; Watanabe, Naohiro [Reprint author]; Shomura, Tomoko; Ohtomo, Hiroshi

CORPORATE SOURCE: Dep. Tropical Med., Jikei Univ. Sch. Med., 3-25-8 Nishishinbashi, Minato-ku, Tokyo 105, Japan

SOURCE: Japanese Journal of Parasitology, (1995) Vol. 44, No. 4, pp. 306-310.

CODEN: KISZAR. ISSN: 0021-5171.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 12 Jan 1996

Last Updated on STN: 12 Jan 1996

AB PF1022A is recently developed as an anthelmintic drug with a structure of cyclic depsipeptide isolated from Mycelia sterilia. Effects of PF1022A were examined in rats infected with Nippostrongylus brasiliensis and in mice infected with Hymenolepis nana. When PF1022A was orally administered for 3 successive days from day 5 post infection (PI) to adults of *N. brasiliensis* in the intestine, almost complete elimination of adult worms was observed at the doses of

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2.5 mg/kg/day or higher. To test the effect on developing larvae in the lung, PF1022A was intraperitoneally administered for 2 days from day 1 PI. No effect was found even at a dose of 10 mg/kg/day. In the case of *H. nana*, PF1022A was orally administered at a dose of 10 mg/kg/day for 2 days from day 5 or day 10 PI to cysticercoids or adult worms, respectively. Similar number of worms was recovered from mice with and without administration of PF1022A. These results suggest that PF1022A is effective against adult *N. brasiliensis* of intestinal phase but not against the larva of tissue phase in rats, and that PF1022A can not eliminate the cysticercoid and the adult of *H. nana* from the intestine of mice.

L21 ANSWER 16 OF 26 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:529792 BIOSIS
DOCUMENT NUMBER: PREV199598544092
TITLE: Effect of PF1022A on adult *Angiostrongylus cantonensis* in the pulmonary arteries and larvae migrating into the central nervous system of rats.
AUTHOR(S): Kachi, S.; Ishih, A.; Terada, M. [Reprint author]
CORPORATE SOURCE: Dep. Parasitol., Hamamatsu Univ. Sch. Med., 3600 Handa-cho, Hamamatsu 431-31, Japan
SOURCE: Parasitology Research, (1995) Vol. 81, No. 8, pp. 631-637.
CODEN: PARREZ. ISSN: 0932-0113.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Dec 1995
Last Updated on STN: 14 Dec 1995

AB We examined the effects of PF1022A, newly developing in Japan, on adult *Angiostrongylus cantonensis* in the pulmonary arteries of rats. Following five and ten successive oral doses at 10 mg/kg per day, the first-stage larvae in rat faeces disappeared completely at 2 weeks after treatment. The treatment completely killed the female worms, but not the male worms. However, numbers of male worms were also decreased after the administration of either five successive oral doses at 10 mg/kg per day for four courses or five successive intraperitoneal doses at 0.5 mg/kg per day. Next, we examined the effects of PF1022A on larval *A. cantonensis* migrating into the central nervous system (CNS) of rats. Following five successive oral doses at 5 or 10 mg/kg per day and five successive intraperitoneal doses at 0.5 mg/kg per day, lesser killing effects were observed on male as well as female worms. On the basis of these results it is apparent that PF1022A will become a promising anthelmintic available as treatment for tissue-dwelling as well as intestinal nematodes.

L21 ANSWER 17 OF 26 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:249708 BIOSIS
DOCUMENT NUMBER: PREV199598264008
TITLE: Effects of PF1022A from Mycelia sterilia on *Trichinella spiralis* in mice.
AUTHOR(S): Wang, Ming [Reprint author]; Watanabe, Naohiro [Reprint author]; Shomura, Tomoko; Ohtomo, Hiroshi [Reprint author]
CORPORATE SOURCE: Dep. Tropical Med., Jikei Univ. Sch. Med., 3-25-8 Nishishinbashi, Minato-ku, Tokyo, Japan
SOURCE: Japanese Journal of Parasitology, (1994) Vol. 43, No. 5, pp. 346-350.
CODEN: KISZAR. ISSN: 0021-5171.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Jun 1995
Last Updated on STN: 11 Jul 1995

Search Results for 10/070387_20061214

AB PF1022A is a cyclic depsipeptide isolated from Mycelia sterilia. The effect of PF1022A was examined by in vivo experiments on adults and larvae of *Trichinella spiralis* in mice. Mice were perorally infected with muscle larvae of *T. spiralis*. In the treatment of adults, PF1022A was orally administered to infected mice for 3 successive days from day 3 post infection (PI) with doses of 10, 2.5, or 0.6mg/kg/day. Complete elimination of adult worms from the intestine was achieved at doses of 10 and 2.5mg/kg/day, and 85% of worms were eliminated by 0.6mg/kg/day. When the drug was intraperitoneally administered with a dose of 5mg/kg/day for day 3-5 PI, no significant effect was observed. In the treatment of muscle larvae, PF1022A at a dose of 20mg/kg/day was given intraperitoneally for 5 successive days to infected mice. A marked reduction (85%) of muscle larvae was obtained only when the administration of drug started at day 14 PI, but no reduction was observed when the administration of drug started at day 21 PI. These results indicate that PF1022A has anthelmintic activity to adults and larvae of *T. spiralis*.

L21 ANSWER 18 OF 26 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1992:387392 BIOSIS
DOCUMENT NUMBER: PREV199294059567; BA94:59567
TITLE: A NEW ANTHELMINTIC CYCLODEPSIPEPTIDE PF1022A.
AUTHOR(S): SASAKI T [Reprint author]; TAKAGI M; YAGUCHI T; MIYADOH S;
OKADA T; KOYAMA M
CORPORATE SOURCE: PHARMACEUTICAL RES LAB, MEIJI SEIKA KAISHA LTD,
MOROOKA-CHO, KOHOKU-KU, YOKOHAMA 222, JPN
SOURCE: Journal of Antibiotics (Tokyo), (1992) Vol. 45, No. 5, pp.
692-697.
CODEN: JANTAJ. ISSN: 0021-8820.

DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

ENTRY DATE: Entered STN: 24 Aug 1992
Last Updated on STN: 1 Oct 1992

AB The novel anthelmintic cyclodepsipeptide PF1022A was isolated from cultured mycelia of Mycelia Sterilia PF1022 (FERM BP-2671). It showed strong anthelmintic activities against Ascaridia galli in chickens. The structure of PF1022A was determined to be cyclo(D-lactyl-L-N-methylleucyl-D-3-phenyllactyl-L-N-methylleucyl-D-lactyl-L-N-methylleucyl-D-3-phenyllactyl-L-N-methylleucyl) by spectroscopic analyses and chemical studies.

L21 ANSWER 19 OF 26 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005463430 EMBASE
TITLE: Influence of the cyclooctadepsipeptides PF1022A and PF1022E as natural products on the design of semi-synthetic anthelmintics such as emodepside.
AUTHOR: Jeschke P.; Iinuma K.; Harder A.; Schindler M.; Murakami T.
CORPORATE SOURCE: P. Jeschke, Bayer CropScience AG, Research and Development, Chemistry Insecticides, Alfred-Nobel-Strasse 50, 40789 Monheim am Rhein, Germany. peter.jeschke@bayercropscience.com
SOURCE: Parasitology Research, (2005) Vol. 97, No. SUPPL. 1, pp. S11-S16.
Refs: 26
ISSN: 0932-0113 CODEN: PARREZ
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology

Search Results for 10/070387_20061214

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 28 Nov 2005

Last Updated on STN: 28 Nov 2005

AB The 24-membered cyclooctadepsipeptide (CODP) PF1022A, the active metabolite of the fungus *imperfectus Mycelia sterilia* (*Rosellinia* sp.) isolated from the plant *Camellia japonica* in Japan, is described as a powerful broad-spectrum anthelmintic natural product with low toxicity in animals. Further CODPs such as PF1022B, C, D and E have been isolated from the same culture and their structures have been established. Both PF1022A and PF1022E serve as valuable starting materials for the synthesis of semi-synthetic CODP derivatives with improved intrinsic anthelmintic potency and broad-spectrum activity. It was found that in most cases the di-substituted PF1022A derivatives showed a greater (or equal) activity by oral application against the gastrointestinal nematode *Haemonchus contortus* compared to the corresponding mono-substituted PF1022A analogues as exemplified by emodepside. In order to get additional information on the bioactive conformation, emodepside was transformed into its mono- and tetra-thionated derivatives by isosteric replacement. In the light of the increased efficacy of these derivatives against *H. contortus* or *Trichostrongylus colubriformis*, it has been suggested that the asymmetric conformation clearly influences the anthelmintic activity of CODPs. Although useful synthetic pathways are available today for the preparation of the semi-synthetic CODP emodepside, the fermentative production of its bis-para-nitro and bis-para-amino precursors could be the process used for its industrial-scale production in the future.

L21 ANSWER 20 OF 26 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005463429 EMBASE

TITLE: Mechanisms of action of emodepside.

AUTHOR: Harder A.; Holden-Dye L.; Walker R.; Wunderlich F.

CORPORATE SOURCE: A. Harder, Bayer HealthCare AG, Animal Health Division, Research and Development, 51368 Leverkusen, Germany.
achim.harder@bayerhealthcare.com

SOURCE: Parasitology Research, (2005) Vol. 97, No. SUPPL. 1, pp. S1-S10.

Refs: 29

ISSN: 0932-0113 CODEN: PARREZ

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

030 Pharmacology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 28 Nov 2005

Last Updated on STN: 28 Nov 2005

AB The research of the class of cyclic octadepsipeptides started at the beginning of the 1990s. PF1022A, the starting material of emodepside, is a natural secondary metabolite of the fungus *Mycelia sterilia*, which belongs to the microflora of the leaves of *Camellia japonica*. PF1022A consists of four N-methyl-L-leucins, two D-lactic acids and two D-phenyllactic acids, which build up a cyclic octadepsipeptide with an alternating L-D-L-configuration. Emodepside is a semisynthetic derivative of PF1022A, which contains a morpholine attached in para position at each of both D-phenyllactic acids. Emodepside is efficacious against a variety of gastrointestinal nematodes. Emodepside binds to a presynaptic latrophilin receptor in nematodes. The

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following presynaptic signal transduction occurs via activation of G α protein and phospholipase-C β , which leads to mobilization of diacylglycerol (DAG). DAG then activates UNC-13 and synaptobrevin, two proteins which play an important role in presynaptic vesicle-functioning. This finally leads to the release of a currently unidentified transmitter. The transmitter (or modulator) exerts its effects at the postsynaptic membrane and induces a flaccid paralysis of the pharynx and the somatic musculature in nematodes.

L21 ANSWER 21 OF 26 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003371509 EMBASE
TITLE: Cyclooctadepsipeptides - An anthelmintically active class of compounds exhibiting a novel mode of action.
AUTHOR: Harder A.; Schmitt-Wrede H.-P.; Krucken J.; Marinovski P.; Wunderlich F.; Willson J.; Amliwala K.; Holden-Dye L.; Walker R.
CORPORATE SOURCE: A. Harder, Bayer AG, BHC, AH-RD-Para, Alfred-Nobel-Str. 50, D-40789 Manheim, Germany. achim.harder.ah@bayer-ag.de
SOURCE: International Journal of Antimicrobial Agents, (1 Sep 2003) Vol. 22, No. 3, pp. 318-331.
Refs: 52
ISSN: 0924-8579 CODEN: IAAGEA
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2003
Last Updated on STN: 25 Sep 2003

AB There are three major classes of anthelmintics for veterinary use: the benzimidazoles/prebenzimidazoles, the tetrahydropyrimidines/imidazothiazoles, and the macrocyclic lactones. In nematodes, there are five targets for the existing anthelmintics: the nicotinic acetylcholine receptor which is the target of tetrahydropyrimidines/imidazothiazoles and indirectly that of the acetylcholinesterase inhibitors; the GABA receptor which is the target of piperazine, the glutamate-gated chloride channel as the target of the macrocyclic lactones, and ss-tubulin as the target of prebenzimidazoles/benzimidazoles. All these anthelmintics are now in serious danger because of the worldwide spread of resistant nematodes in sheep, cattle, horses and pigs. The class of cyclooctadepsipeptides has entered the scene of anthelmintic research in the early 1990s. PF1022A, the first anthelmintically active member, is a natural compound from the fungus Mycelia sterilia that belongs to the microflora of the leaves of the Camellia japonica. PF1022A contains 4 N-Methyl-L-leucines, 2 D-lactic acids and 2-D-phenyllactic acids arranged as a cyclic octadepsipeptide with an alternating L-D-L-configuration. Emodepside is a semisynthetic derivative of PF1022A with a morpholine ring at each of the two D-phenyllactic acids in para position. The anthelmintic activity is directed against gastrointestinal nematodes in chicken, mice, rats, meriones, dogs, cats, sheep, cattle and horses. Moreover, emodepside is active against *Trichinella spiralis* larvae in muscles, microfilariae and preadult filariae and *Dictyocaulus viviparus*. PF1022A and emodepside are fully effective against benzimidazole-, levamisole or ivermectin-resistant nematodes in sheep and cattle. In *Ascaris suum* both cyclooctadepsipeptides lead to paralysis indicating a neuropharmacological action of these compounds. Using a PF1022A-ligand immunoscreening of a cDNA library from *Haemonchus contortus* a cDNA clone of 3569 base pairs could be identified. This clone codes for a novel 110

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kDa heptahelical transmembrane receptor, named HC110R. Database- and phylogenetic analysis reveals that this receptor is a homolog to B0457.1 from *Caenorhabditis elegans* and has significant similarity to latrophilins from human, cattle and rat. HC110R is located in the plasma membrane and in lysosomes and endosomes. α -Latrotoxin, the poison of the black widow spider, binds at a 54 kDa aminoterminal fragment of HC110R. After binding a Ca(2+)-influx into HEK293 cells is induced which can be blocked by EGTA, Cd(2+) or nifedipine. PF1022A or emodepside also bind to this 54 kDa aminoterminal region of HC110R and interact with the functional responses of α -latrotoxin. In *C. elegans* antibodies against the C- or N-terminus of HC110R bind to the B0457.1 protein located in the pharynx. Electrophysiological studies reveal that emodepside inhibits pharyngeal pumping of the nematodes in a concentration dependent way with an IC(50) value of about 4 nM. Thus, it is tempting to speculate that emodepside exerts its action on nematodes via a latrophilin-like receptor which might have an important regulatory function on pharyngeal pumping. .COPYRGT. 2003 Elsevier B.V. and the International Society of Chemotherapy. All rights reserved.

- L21 ANSWER 22 OF 26 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
- ACCESSION NUMBER: 2002095183 EMBASE
- TITLE: Use of network analysis of metabolic systems in bioengineering.
- AUTHOR: Schuster S.; Klamt S.; Weckwerth W.; Moldenhauer F.; Pfeiffer T.
- CORPORATE SOURCE: S. Schuster, Department of Bioinformatics, Max Delbrück Ctr. for Molec. Med., 13092 Berlin-Buch, Germany.
stschust@mdc-berlin.de
- SOURCE: Bioprocess and Biosystems Engineering, (2001) Vol. 24, No. 6, pp. 363-372. .
Refs: 43
ISSN: 1615-7591 CODEN: BBEIBV
- COUNTRY: Germany
- DOCUMENT TYPE: Journal; Article
- FILE SEGMENT: 004 Microbiology
- LANGUAGE: English
- SUMMARY LANGUAGE: English
- ENTRY DATE: Entered STN: 21 Mar 2002
Last Updated on STN: 21 Mar 2002
- AB Basic ideas and recent developments in network analysis of metabolic systems and various applications of this analysis in bioengineering are reviewed. Central concepts are the null-space to the stoichiometry matrix and the elementary flux modes. The applicability of elementary-modes analysis in biotechnology is illustrated by the synthesis of the cyclooctadepsipeptides PF1022 in the fungus *Mycelia sterilia*. Network analysis is also useful in metabolic flux analysis. In particular, a procedure for finding out which reaction rates can be uniquely calculated in underdetermined reaction networks is outlined. The concept of 'enzyme subsets' is explained and its use for analysing genetic regulation is demonstrated. In particular, the correlation between expression data concerning the diauxic shift in yeast and the enzyme subsets in yeast metabolism is discussed.
- L21 ANSWER 23 OF 26 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
- ACCESSION NUMBER: 92179424 EMBASE
- DOCUMENT NUMBER: 1992179424
- TITLE: A new anthelmintic cyclodepsipeptide, PF1022A.
- AUTHOR: Sasaki T.; Takagi M.; Yaguchi T.; Miyadoh S.; Okada T.; Koyama M.
- CORPORATE SOURCE: Pharmaceutical Research Laboratories, Meiji Seika Kaisha

Search Results for 10/070387_20061214

SOURCE: Ltd, Morooka-cho, Kohoku-ku, Yokohama 222, Japan
 Journal of Antibiotics, (1992) Vol. 45, No. 5, pp. 692-697.

COUNTRY: ISSN: 0021-8820 CODEN: JANTAJ

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

030 Pharmacology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 19 Jul 1992

Last Updated on STN: 19 Jul 1992

AB The novel anthelmintic cyclodepsipeptide PF1022A was isolated from cultured mycelia of Mycelia Sterilia PF1022 (FERM BP-2671). It showed strong anthelmintic activities against Ascaridia galli in chickens. The structure of PF1022A was determined to be cyclo(D-lactyl-L-N-methylleucyl-D-3-phenyllactyl-L-N-methylleucyl-D-lactyl-N-methylleucyl-D-3-phenyllactyl-L-N-methylleucyl) by spectroscopic analyses and chemical studies.

L21 ANSWER 24 OF 26 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-018934 [01] WPIDS

DOC. NO. CPI: C2003-004701 [01]

TITLE: Novel biosynthesis gene-transferred transformants for producing PF1022 substance derivatives by fermentation, as pharmaceuticals or veterinary drugs with anthelmintic activity

DERWENT CLASS: B04; D16

INVENTOR: MORIYA T; MURAKAMI T; SUMIDA N; WATANABE M; YANAI K

PATENT ASSIGNEE: (MEIJ-C) MEIJI SEIKA KAISHA LTD; (MEIJ-C) MEIJISEIKA KAISHA LTD; (MORI-I) MORIYA T; (MURA-I) MURAKAMI T;

(SUMI-I) SUMIDA N; (WATA-I) WATANABE M; (YANA-I) YANAI K

COUNTRY COUNT: 99

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002077244	A1	20021003	(200301)*	JA	116 [21]	
NO 2003004072	A	20031119	(200382)	NO		
EP 1380649	A1	20040114	(200410)	EN		
KR 2003093244	A	20031206	(200425)	KO		
AU 2002241272	A1	20021008	(200432)	EN		
JP 2002576686	X	20040715	(200446)	JA		
CN 1509334	A	20040630	(200462)	ZH		
US 20040214274	A1	20041028	(200471)	EN		
NZ 528268	A	20050527	(200537)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002077244	A1	WO 2002-JP2782	20020322
AU 2002241272	A1	AU 2002-241272	20020322
CN 1509334	A	CN 2002-810040	20020322
EP 1380649	A1	EP 2002-707130	20020322
JP 2002576686	X	JP 2002-576686	20020322
NZ 528268	A	NZ 2002-528268	20020322
NO 2003004072	A	WO 2002-JP2782	20020322
EP 1380649	A1	WO 2002-JP2782	20020322
JP 2002576686	X	WO 2002-JP2782	20020322

Search Results for 10/070387_20061214

US 20040214274 A1
 NZ 528268 A
 NO 2003004072 A
 KR 2003093244 A
 US 20040214274 A1

WO 2002-JP2782 20020322
 WO 2002-JP2782 20020322
 NO 2003-4072 20030915
 KR 2003-712092 20030916
 US 2003-472587 20030922

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1380649 A1	Based on	WO 2002077244 A
AU 2002241272 A1	Based on	WO 2002077244 A
JP 2002576686 X	Based on	WO 2002077244 A
NZ 528268 A	Based on	WO 2002077244 A

PRIORITY APPLN. INFO: JP 2001-82227 20010322

AN 2003-018934 [01] WPIDS

AB WO 2002077244 A1 UPAB: 20060118

NOVELTY - A transformant capable of producing PF1022 substance derivatives is obtained by transferring a gene participating in the biosynthesis pathway from chorismic acid to p-aminophenylpyruvic acid (biosynthesis gene) into a phenylalanine-requiring host derived from an organism producing the PF1022 substance of formula (I).

DETAILED DESCRIPTION - A transformant capable of producing PF1022 substance derivatives is obtained by transferring a gene participating in the biosynthesis pathway from chorismic acid to p-aminophenylpyruvic acid (biosynthesis gene) into a phenylalanine-requiring host derived from an organism producing the PF1022 substance of formula (I).

(I) INDEPENDENT CLAIMS are also included for:

(1) a process for producing PF1022 substance derivatives by culturing the transformants before collecting the product;
 (2) a polynucleotide encoding an amino acid sequence of (XXXVII) of 263 amino acids, or its modified sequence having chorismate mutase activity; and

(3) a polynucleotide encoding an amino acid sequence of (XXXVIII) of 378 amino acids, or its modified sequence having prephenate dehydratase (sic) activity.

ACTIVITY - Anthelmintic.

MECHANISM OF ACTION - None given in source material.

USE - The transformants are producing PF1022 substance derivatives by fermentation, for use as pharmaceuticals or veterinary drugs.

ADVANTAGE - With the transformants, the PF1022 substance derivatives e.g. PF1022-220 and PF1022-260 can be obtained by a direct fermentation method.

L21 ANSWER 25 OF 26	WPIDS COPYRIGHT 2006	THE THOMSON CORP on STN
ACCESSION NUMBER:	2001-290517 [30]	WPIDS
DOC. NO. CPI:	C2001-088988 [30]	
TITLE:	Transformant producing secondary metabolite modified with functional group e.g. benzene with nitrogen-containing substituent at para-position, PF1022, with ease at low cost, for application in pharmaceuticals and agrochemicals	
DERWENT CLASS:	B04; D16	
INVENTOR:	MIDOH N; MIDOH N P T L; MIYAMOTO K; MIYAMOTO K P T L; MURAKAMI T; MURAKAMI T P T L; OKAKURA K; OKAKURA K P T L; WATANABE M; WATANABE M P T L; YANAI K; YANAI K P T L; YASUDA S; YASUDA S P T L	
PATENT ASSIGNEE:	(MEIJ-C) MEIJI SEIKA CO; (MEIJ-C) MEIJI SEIKA KAISHA LTD	
COUNTRY COUNT:	93	

Search Results for 10/070387_20061214

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001023542	A1	20010405	(200130)*	JA	83[13]	
AU 2000074496	A	20010430	(200142)	EN		
NO 2002001549	A	20020527	(200247)	NO		
EP 1223215	A1	20020717	(200254)	EN		
KR 2002064788	A	20020809	(200309)	KO		
CN 1377407	A	20021030	(200314)	ZH		
JP 2001526925	X	20030415	(200328)	JA		
NZ 518551	A	20030926	(200366)	EN		
AU 783603	B2	20051110	(200634)	EN		
US 7109018	B1	20060919	(200662)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001023542	A1	WO 2000-JP6783	20000929
AU 2000074496	A	AU 2000-74496	20000929
AU 783603	B2	AU 2000-74496	20000929
CN 1377407	A	CN 2000-813681	20000929
EP 1223215	A1	EP 2000-962989	20000929
NZ 518551	A	NZ 2000-518551	20000929
NO 2002001549	A	WO 2000-JP6783	20000929
EP 1223215	A1	WO 2000-JP6783	20000929
JP 2001526925	X	WO 2000-JP6783	20000929
NZ 518551	A	WO 2000-JP6783	20000929
JP 2001526925	X	JP 2001-526925	20000929
KR 2002064788	A	KR 2002-704056	20020328
NO 2002001549	A	NO 2002-1549	20020402
US 7109018	B1	WO 2000-JP6783	20000929
US 7109018	B1	US 2002-89514	20020329

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000074496	A	Based on
EP 1223215	A1	Based on
JP 2001526925	X	Based on
NZ 518551	A	Based on
AU 783603	B2	Based on
US 7109018	B1	Based on

PRIORITY APPLN. INFO: JP 1999-276314 19990929

AN 2001-290517 [30] WPIDS

AB WO 2001023542 A1 UPAB: 20060117

NOVELTY - A transformant having been modified produces a secondary metabolite having a benzene ring skeleton free from substitution at the para-position by a nitrogen-containing functional group, thereby enabling the production of a secondary metabolite with a benzene ring skeleton substituted at the para-position by a nitrogen-containing group.

DETAILED DESCRIPTION - A transformant is a transformant of an organism which produces a secondary metabolite having a benzene ring skeleton free from substitution at the para-position by a nitrogen-containing functional group, which has been transformed by transferring a gene participating in the biosynthesis pathway from chorismic acid into p-aminophenylpyruvic acid thereby enabling the production of a secondary metabolite with a benzene ring skeleton

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substituted at the para-position by a nitrogen-containing group. Such transformant can produce a secondary metabolite modified with functional group e.g. benzene with nitrogen-containing substituent at para-position with ease at low cost.

INDEPENDENT CLAIMS are also included for;

(i) a process for producing the secondary metabolite by culturing the transformant before isolating the product;

(ii) a polynucleotide encoding an amino-acid sequence of SEQ ID NO:2, or its modified sequence with 4-amino-4-deoxychorismic acid synthase activity;

(iii) a polynucleotide encoding an amino-acid sequence of SEQ ID NO:4, or its modified sequence with 4-amino-4-deoxychorismic acid mutase activity; and

(iv) a polynucleotide encoding an amino-acid sequence of SEQ ID NO:6, or its modified sequence with 4-amino-4-deoxyprephenic acid dehydrogenase activity.

USE - The transformant is used e.g. to produce PF1022 for application in pharmaceuticals, veterinary drugs and agrochemicals.

ADVANTAGE - The transformant can produce a secondary metabolite modified with functional group e.g. benzene with nitrogen-containing substituent at para-position with ease at low cost.

DESCRIPTION OF DRAWINGS - A diagram showing the restriction enzyme map and positions of open-reading frames of a DNA fragment isolated from *Streptomyces venezuelae*. (Drawing includes non-English language text).

L21 ANSWER 26 OF 26	WPIDS COPYRIGHT 2006	THE THOMSON CORP on STN
ACCESSION NUMBER:	2001-265970 [27]	WPIDS
DOC. NO. CPI:	C2001-080505 [27]	
TITLE:	Novel cyclic depsipeptide synthase and gene encoding it for efficient production of anthelmintic substance	
PF1022		
DERWENT CLASS:	B03; B04; D16	
INVENTOR:	AIHARA S; FUTAMURA T; KLEINKAUF H; MIDOH N; MIDOH N O K; MIYAMOTO K; MURAKAMI T; OKAKURA K; WATANABE M; YANAI K; YASUTAKE T; AIHARA P T; AIHARA S P T L; FUTAMURA P T; FUTAMURA T P T L; KLEINKAUF H T U B; KLEINKAUF T U; MIDOH N P T L; MIDOH P T; MIYAMOTO K P T L; MIYAMOTO P T; MURAKAMI P T; MURAKAMI T P T L; OKAKURA K P T L; OKAKURA P T; WATANABE M P T L; WATANABE P T; YANAI K P T L; YANAI P T; YASUTAKE P T; YASUTAKE T P T L	
PATENT ASSIGNEE:	(MEIJ-C) MEIJI SEIKA KAISHA LTD; (MEIJ-C) MEIJI SEIKA KK	
COUNTRY COUNT:	93	

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
<hr/>						
WO 2001018179	A1	20010315	(200127)*	JA	92[4]	
AU 2000068741	A	20010410	(200137)	EN		
NO 2002001100	A	20020507	(200239)	NO		
EP 1215281	A1	20020619	(200240)	EN		
KR 2002029767	A	20020419	(200269)	KO		
CN 1387566	A	20021225	(200324)	ZH		
JP 2001522391	X	20030402	(200325)	JA		
NZ 517588	A	20050128	(200513)	EN		
CN 1183248	C	20050105	(200620)	ZH		
EP 1215281	B1	20060524	(200635)	EN		
DE 60028217	E	20060629	(200643)	DE		
AU 784466	B2	20060406	(200674)	EN		

APPLICATION DETAILS:

Search Results for 10/070387_20061214

PATENT NO	KIND	APPLICATION	DATE
WO 2001018179 A1		WO 2000-JP6103	20000907
AU 2000068741 A		AU 2000-68741	20000907
CN 1387566 A		CN 2000-815301	20000907
CN 1183248 C		CN 2000-815301	20000907
DE 60028217 E		DE 2000-628217	20000907
EP 1215281 A1		EP 2000-957009	20000907
EP 1215281 B1		EP 2000-957009	20000907
DE 60028217 E		EP 2000-957009	20000907
NZ 517588 A		NZ 2000-517588	20000907
NO 2002001100 A		WO 2000-JP6103	20000907
EP 1215281 A1		WO 2000-JP6103	20000907
JP 2001522391 X		WO 2000-JP6103	20000907
NZ 517588 A		WO 2000-JP6103	20000907
EP 1215281 B1		WO 2000-JP6103	20000907
DE 60028217 E		WO 2000-JP6103	20000907
JP 2001522391 X		JP 2001-522391	20000907
KR 2002029767 A		KR 2002-702704	20020228
NO 2002001100 A		NO 2002-1100	20020306
AU 784466 B2		AU 2000-68741	20000907

FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 60028217	E	Based on
AU 2000068741	A	Based on
EP 1215281	A1	Based on
JP 2001522391	X	Based on
NZ 517588	A	Based on
EP 1215281	B1	Based on
DE 60028217	E	Based on
AU 784466	B2	Based on
		EP 1215281 A
		WO 2001018179 A
		WO 2001018179 A
		WO 2001018179 A
		WO 2001018179 A
		WO 2001018179 A
		WO 2001018179 A
		WO 2001018179 A

PRIORITY APPLN. INFO: JP 2000-104291 20000406
JP 1999-253040 19990907

AN 2001-265970 [27] WPIDS

AB WO 2001018179 A1 UPAB: 20050901

NOVELTY - Cyclic depsipeptide synthase (sequence given, 3210 residues) originating in *Mycelia sterilia* or derived from this sequence by addition, deletion and/or substitution of one or more amino acid residues, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) cover DNA encoding the synthase;
- (2) expression vectors incorporating the DNA;
- (3) host cells transformed by the vectors; and
- (4) preparation of the synthase and/or a cyclic depsipeptide by culture of the transformants.

USE - Efficient production of the anthelmintic PF1022 (cyclo(D-lactyl-L-N-methylleucyl-D-3-phenyllactyl-L-N-methylleucyl-D-lactyl-L-N-methylleucyl-D-3-phenyllactyl-L-N-methylleucyl)).

L16 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:439221 CAPLUS
DOCUMENT NUMBER: 144:466569
TITLE: Biosynthesis of unnatural organic substances by transgenic filamentous fungi. Powerful fermentative production of next-generation vermicides employing metabolic engineering
AUTHOR(S): Yanai, Koji
CORPORATE SOURCE: Microbiological Resources and Technology Laboratories, Meiji Seika Kaisha, Ltd., Japan
SOURCE: Kagaku to Seibutsu (2006), 44(4), 222-224
CODEN: KASEAA; ISSN: 0453-073X
PUBLISHER: Gakkai Shuppan Senta
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review on fermentative production of unnatural para-position derivs. of PF1022A, a fungal anthelmintic cyclodepsipeptide, by transgenic *Rosellinia* sp. PF1022 with *Streptomyces venezuelae* antibiotic biosynthesis pap genes.

L16 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:527718 CAPLUS
DOCUMENT NUMBER: 141:242096
TITLE: Para-position derivatives of fungal anthelmintic cyclodepsipeptides engineered with *Streptomyces venezuelae* antibiotic biosynthetic genes
AUTHOR(S): Yanai, Koji; Sumida, Naomi; Okakura, Kaoru; Moriya, Tatsuki; Watanabe, Manabu; Murakami, Takeshi
CORPORATE SOURCE: Microbiological Resources and Technology Laboratories, Meiji Seika Kaisha, Ltd., Odawara-shi, Kanagawa, 250-0852, Japan
SOURCE: Nature Biotechnology (2004), 22(7), 848-855
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PF1022A, a cyclooctadepsipeptide possessing strong anthelmintic properties and produced by the filamentous fungus *Rosellinia* sp. PF1022, consists of four alternating residues of N-methyl-L-leucine and four residues of D-lactate or D-phenyllactate. PF1022A derivs. obtained through modification of their benzene ring at the para-position with nitro or amino groups act as valuable starting materials for the synthesis of compds. with improved anthelmintic activities. Here we describe the production of such derivs. by fermentation through metabolic engineering of the PF1022A biosynthetic pathway in *Rosellinia* sp. PF1022. Three genes cloned from *Streptomyces venezuelae*, and required for the biosynthesis of p-aminophenylpyruvate from chorismate in the chloramphenicol biosynthetic pathway, were expressed in a chorismate mutase-deficient strain derived from *Rosellinia* sp. PF1022. Liquid chromatog.-mass spectrometry and NMR analyses confirmed that this approach facilitated the production of PF1022A derivs. specifically modified at the para-position. This fermentation method is

environmentally safe and can be used for the industrial scale production of PF1022A derivs.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Search Results for 10/070387_20061214

ACCESSION NUMBER: 2002:754596 CAPLUS
 DOCUMENT NUMBER: 137:274081
 TITLE: Biosynthetic production of PF1022 derivatives using p-aminophenyl pyruvate biosynthesis pathway enzymes
 INVENTOR(S): Yanai, Koji; Sumida, Naomi; Watanabe, Manabu; Moriya, Tatsuki; Murakami, Takeshi
 PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
 SOURCE: PCT Int. Appl., 116 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002077244	A1	20021003	WO 2002-JP2782	20020322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2441346	AA	20021003	CA 2002-2441346	20020322
EP 1380649	A1	20040114	EP 2002-707130	20020322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1509334	A	20040630	CN 2002-810040	20020322
NZ 528268	A	20050527	NZ 2002-528268	20020322
NO 2003004072	A	20031119	NO 2003-4072	20030915
US 2004214274	A1	20041028	US 2003-472587	20030922
PRIORITY APPLN. INFO.:			JP 2001-82227	A 20010322
			WO 2002-JP2782	W 20020322

AB A direct fermentation method for biosynthetic production of PF1022 derivs. (in particular, PF1022-220 and PF1022-260) by transformation of PF1022-producing microorganism with genes coding for enzymes involved in the biosynthesis of p-aminophenyl pyruvate from chorismic acid, is provided. Phenylalanine-dependent microorganisms, *Mycelia sterilia* FERM BP-2671, in particular, lacking the endogenous chorismate mutase and/or prephenate dehydrogenase activities, are transformed. *Streptomyces venezuelae* genes papA, papB, and papC, coding for 4-amino-4-deoxychorismate synthase, 4-amino-4-deoxychorismate mutase, and 4-amino-4-deoxyprephenate dehydrogenase, resp., were cloned and used to transform *Mycelia sterilia* FERM BP-2671, whose endogenous chorismate mutase and/or prephenate dehydrogenase activities destroyed via homologous recombination. Production of PF1022-220 and PF1022-260, in *Mycelia sterilia*, transformed with papA, papB, and papC genes, was observed

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:798412 CAPLUS
 DOCUMENT NUMBER: 135:340830
 TITLE: *Mycelia sterilia* (R)-2-hydroxy-3-phenylpropionate (D-phenyllactate) dehydrogenase and cDNA
 INVENTOR(S): Miyamoto, Koichi; Sumida, Naomi; Midoh,

Search Results for 10/070387 20061214

PATENT ASSIGNEE(S): Naoki; Murakami, Takeshi; Zocher,
Rainer; Kleinkauf, Horst
Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081563	A1	20011101	WO 2001-JP3645	20010426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2407059	AA	20011101	CA 2001-2407059	20010426
AU 2001052608	A5	20011107	AU 2001-52608	20010426
EP 1291417	A1	20030312	EP 2001-925976	20010426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 522584	A	20040227	NZ 2001-522584	20010426
NO 2002005126	A	20021220	NO 2002-5126	20021025
US 2003186410	A1	20031002	US 2002-258472	20021107
US 6916641	B2	20050712		

PRIORITY APPLN. INFO.: JP 2000-125449 A 20000426
WO 2001-JP3645 W 20010426

AB A D-phenyllactate dehydrogenase (D-PLDH) of *Mycelia sterilia*, gene, recombinant expression, and use in enzymic synthesis of D-phenyllactate, PF1022, or their derivs., are disclosed. Cloning of D-PLDH cDNA from *Mycelia sterilia* FERM BP-2671 and recombinant expression in *E. coli*, are described. Production of D-phenyllactate from Ph pyruvate was demonstrated. Pyruvate was also used as a substrate, though the activity was only 10% of that with Ph pyruvate as substrate.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT.

L16 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:247475 CAPLUS

DOCUMENT NUMBER: 134:277400

TITLE: *Streptomyces venezuelae* genes *papA*, *papB*, and *papC*, coding for 4-amino-4-deoxychorismate synthase, 4-amino-4-deoxychorismate mutase, and 4-amino-4-deoxyprephenate dehydrogenase, recombinant expression, and use in biosynthesis of para-amino or nitro substituted benzene ring-containing compound

INVENTOR(S) : Yanai, Koji; Okakura, Kaoru;
Yasuda, Shohei; Watanabe, Manabu;
Miyamoto, Koichi; Midoh, Naoki;
Murakami, Takeshi

PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023542	A1	20010405	WO 2000-JP6783	20000929
W: AE, AG, AL, AM, AT, AU, AZ, CR, CU, CZ, DE, DK, DM, DZ, HU, ID, IL, IN, IS, JP, KE, LU, LV, MA, MD, MG, MK, MN, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, YU, ZA, ZW			BA, BB, BG, BR, BY, BZ, CA, CH, CN, EE, ES, FI, GB, GD, GE, GH, GM, HR, KG, KP, KR, KZ, LC, LK, LR, LS, LT, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, TG	
RW: GH, GM, KE, LS, MW, MZ, SD, CA 2386255		20010405	CA 2000-2386255	20000929
AU 2000074496	A5	20010430	AU 2000-74496	20000929
AU 783603	B2	20051110		
EP 1223215	A1	20020717	EP 2000-962989	20000929
R: AT, BE, CH, DE, DK, ES, FR, IE, SI, LT, NZ 518551			GB, GR, IT, LI, LU, NL, SE, MC, PT, LV, FI, RO, MK, CY, AL	
US 7109018	B1	20060919	NZ 2000-518551	20000929
NO 2002001549	A	20020527	US 2002-89514	20020329
PRIORITY APPLN. INFO.:			NO 2002-1549	20020402
			JP 1999-276314	A 19990929
			WO 2000-JP6783	W 20000929

AB Microorganisms genetically engineered to produce a secondary metabolite wherein a benzene ring substituted at the para-position with a nitrogen-containing functional group, nitro or amino group, in particular, are disclosed. A microorganism, Streptomyces, Nocardia, or Corynebacteria, in particular, which produces a secondary metabolite having a benzene ring skeleton free from substitution at the para-position by a nitrogen-containing functional group, are transformed with genes participating in the biosynthesis of p-aminophenylpyruvic acid from chorismic acid so as to enable the production of a secondary metabolite having a benzene ring skeleton substituted at the para-position by a nitrogen-containing functional group. Biosynthesis of Ph pyruvic acid, p-hydroxyphenyl lactate, phenylalanine, tyrosine, or Ph lactate in those microorganisms are claimed. Biosynthesis of peptides and cyclic depsipeptides, in particular PF1022 derivs., are also claimed. Also, novel genes participating in the biosynthesis of p-aminophenylpyruvic acid from chorismic acid are provided. Streptomyces venezuelae genes papA, papB, and papC, coding for 4-amino-4-deoxychorismate synthase, 4-amino-4-deoxychorismate mutase, and 4-amino-4-deoxyprephenate dehydrogenase, resp., are claimed. Synthesis of 4-amino-4-deoxychorismate was detected in E. coli transformed with papA gene. Reduction in the amount of 4-amino-4-deoxychorismate and increase in the amount of 4-Amino-4-deoxyprephenate was observed in E. coli transformed with papB gene. Reduction in the amount of 4-amino-4-deoxychorismate and 4-amino-4-deoxyprephenate and increase in the amount of p-phenylalanine, the product of aminotransferase reaction on p-aminophenyl pyruvate, was observed in E. coli transformed with papC gene. Production of PF1022-268, cyclo[MeLeu-Lac-MeLeu-(O2N)PhLac-MeLeu-Lac-MeLeu-PhLac], PF1022-269, and cyclo[MeLeu-Lac-MeLeu-(H2N)PhLac-MeLeu-Lac-MeLeu-PhLac] in Mycelia sterilia, transformed with papA, papB, and papC genes, was observed

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:185930 CAPLUS

DOCUMENT NUMBER: 134:218008

TITLE: DNA sequence of the promoter and the terminator of Abp1 gene of Mycelia sterilia and the its regulation for transcription

Search Results for 10/070387_20061214

INVENTOR(S): Watanabe, Manabu; Murakami, Takeshi
 PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
 SOURCE: PCT Int. Appl., 26 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018219	A1	20010315	WO 2000-JP6104	20000907
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2384000	AA	20010315	CA 2000-2384000	20000907
AU 2000068742	A5	20010410	AU 2000-68742	20000907
AU 782525	B2	20050804		
EP 1221489	A1	20020710	EP 2000-957010	20000907
EP 1221489	B1	20061129		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NZ 517463	A	20031031	NZ 2000-517463	20000907
US 6913905	B1	20050705	US 2002-70386	20000907
NO 2002000941	A	20020506	NO 2002-941	20020227
PRIORITY APPLN. INFO.:			JP 1999-252851	A 19990907
			WO 2000-JP6104	W 20000907

AB This invention provides an endogenous gene promoter in filamentous fungi (*Mycfelia sterilia*) which has high transcription efficiency. A highly expressed gene (Abp1) was isolated from *Mycfelia sterilia* (PF 1022) by randomly sequencing the clones in cDNA library and its genomic DNA was also isolated which containing promoter and terminator region. The reporter gene was highly expressed under Abp1 gene promoter when transformed into *Mycfelia sterilia* (PF1022).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:185893 CAPLUS
 DOCUMENT NUMBER: 134:218924
 TITLE: *Mycelia sterilia cyclic depsipeptide synthase, gene, recombinant expression, and use in cyclic depsipeptide biosynthesis*
 INVENTOR(S): Midoh, Naoki; Okakura, Kaoru;
 Miyamoto, Koichi; Watanabe, Manabu;
 Yanai, Koji; Yasutake, Tetsuya;
 Aihara, Sato; Futamura, Takafumi;
 Kleinkauf, Horst; Murakami, Takeshi
 PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
 SOURCE: PCT Int. Appl., 92 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

Search Results for 10/070387_20061214

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018179	A1	20010315	WO 2000-JP6103	20000907
W: AE, AG, AL, AM, AT, AU, AZ, CR, CU, CZ, DE, DK, DM, DZ, HU, ID, IL, IN, IS, JP, KE, LU, LV, MA, MD, MG, MK, MN, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, DE, DK, ES, FI, FR, GB, GR, CF, CG, CI, CM, GA, GN, GW,		BA, BB, BG, BR, BY, BZ, CA, CH, CN, EE, ES, FI, GB, GD, GE, GH, GM, HR, KG, KP, KR, KZ, LC, LK, LR, LS, LT, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, ML, MR, NE, SN, TD, TG		
CA 2384122	AA	20010315	CA 2000-2384122	20000907
EP 1215281	A1	20020619	EP 2000-957009	20000907
EP 1215281	B1	20060524		
R: AT, BE, CH, DE, DK, ES, FR, IE, SI, LT, LV, FI, RO, MK,		GB, GR, IT, LI, LU, NL, SE, MC, PT, CY, AL		
NZ 517588	A	20050128	NZ 2000-517588	20000907
AU 784466	B2	20060406	AU 2000-68741	20000907
AT 327321	E	20060615	AT 2000-957009	20000907
NO 2002001100	A	20020507	NO 2002-1100	20020306
PRIORITY APPLN. INFO.:				
		JP 1999-253040	A 19990907	
		JP 2000-104291	A 20000406	
		WO 2000-JP6103	W 20000907	

AB Enzymes synthesizing cyclic depsipeptides (in particular a substance PF1022), and genes, are disclosed. Moreover, a mass production system of a cyclic depsipeptide, a process for recombinant expression of a cyclic depsipeptide synthase, are provided. PF1022A belongs to a recently identified class of N-methylated cyclooctadepsipeptides (CODPs) with strong anthelmintic properties. Described here is the cell-free synthesis of this CODP and related structures, as well as the purification and enzymic characterization of the responsible synthetase. Four PF1022A synthesis exts. of Mycelia sterilia were incubated with the precursors L-leucine, D-lactate, D-phenyllactate, and S-adenosyl-L-methionine in the presence of ATP and MgCl₂. A 350-kDa depsipeptide synthetase, PFSYN, responsible for PF1022A synthesis was purified to electrophoretic homogeneity. Like other peptide synthetases, PFSYN follows a thiotemplate mechanism in which the substrates are activated as thioesters via adenylation. N-Methylation of the substrate L-leucine takes place after covalent binding prior to peptide bond formation. The enzyme is capable of synthesizing all known natural cyclooctadepsipeptides of the PF1022 type (A, B, C, and D) differing in the content of D-lactate and D-phenyllactate. In addition to PF1022 types A, B, C, and D, the in vitro incubations produced PF1022F (a CODP consisting of D-lactate and N-methyl-L-leucine), as well as di-, tetra-, and hexa-PF1022 homologs. PFSYN strongly resembles the well documented enniatin synthetase in size and mechanism. The results suggest that PFSYN, like enniatin synthetase, is an enzyme with two peptide synthetase domains and forms CODP by repeated condensation of dipeptidol building blocks. Due to the low specificity of the D-hydroxy acid binding site, D-lactate or D-phenyllactate can be incorporated into the dipeptidols depending on the concentration of these substrates in the reaction mixture

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2000:412788 CAPLUS
 DOCUMENT NUMBER: 133:219266
 TITLE: Biosynthesis of PF1022A and related cyclooctadepsipeptides
 AUTHOR(S): Weckwerth, Wolfram; Miyamoto, Koichi;

Search Results for 10/070387_20061214

Iinuma, Katsuhura; Krause, Martin; Glinski, Mirko;
Storm, Thomas; Bonse, Gerd; Kleinkauf, Horst
; Zocher, Rainer
CORPORATE SOURCE: Max-Volmer-Institut fur Biophysikalische Chemie und
Biochemie, Technische Universitat Berlin, Berlin,
D-10587, Germany
SOURCE: Journal of Biological Chemistry (2000), 275(23),
17909-17915
CODEN: JBCHA3; **ISSN:** 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular
Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PF1022A belongs to a recently identified class of N-methylated cyclooctadepsipeptides (CODPs) with strong anthelmintic properties. Described here is the cell-free synthesis of this CODP and related structures, as well as the purification and enzymic characterization of the responsible synthetase. For PF1022A synthesis exts. of Mycelia sterilia were incubated with the precursors L-leucine, D-lactate, D-phenyllactate, and S-adenosyl-L-methionine in the presence of ATP and MgCl₂. A 350-kDa depsipeptide synthetase, PFSYN, responsible for PF1022A synthesis was purified to electrophoretic homogeneity. Like other peptide synthetases, PFSYN follows a thiotemplate mechanism in which the substrates are activated as thioesters via adenylation. N-Methylation of the substrate L-leucine takes place after covalent binding prior to peptide bond formation. The enzyme is capable of synthesizing all known natural cyclooctadepsipeptides of the PF1022 type (A, B, C, and D) differing in the content of D-lactate and D-phenyllactate. In addition to PF1022 types A, B, C, and D, the in vitro incubations produced PF1022F (a CODP consisting of D-lactate and N-methyl-L-leucine), as well as di-, tetra-, and hexa-PF1022 homologs. PFSYN strongly resembles the well documented enniatin synthetase in size and mechanism. Our results suggest that PFSYN, like enniatin synthetase, is an enzyme with two peptide synthetase domains and forms CODP by repeated condensation of dipeptidol building blocks. Due to the low specificity of the D-hydroxy acid binding site, D-lactate or D-phenyllactate can be incorporated into the dipeptidols depending on the concentration of these substrates in the reaction mixture
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:151554 CAPLUS
DOCUMENT NUMBER: 126:156481
TITLE: Recombinant preparation of anthelmintic substance PF1022 using transformed hyphomycetes strain PF1022
INVENTOR(S): Aoyagi, Kaoru; Watanabe, Manabu; Yanai, Kohji; Murakami, Takeshi
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9700944 W: JP, US	A1	19970109	WO 1996-JP1692	19960619

Search Results for 10/070387_20061214

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP 780468 A1 19970625 EP 1996-918848 19960619
R: DE, ES, FR, GB
US 5763221 A 19980609 US 1997-776816 19970207
PRIORITY APPLN. INFO.: JP 1995-155973 A 19950622
WO 1996-JP1692 W 19960619

AB A method for transforming strain PF1022, which produces a cyclic depsipeptide (substance PF1022) and belongs to Agonomycetales of the class Hyphomycetes, by using a plasmid consisting of a promoter, a terminator, a marker gene and the gene associated with the biosynthesis of PF1022. As a result, the utilization of nutrients by the transformant and its cyclic depsipeptide productivity are improved.

Search Results for 10/070387_20061214

L25 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
 ACCESSION NUMBER: 1998:112356 CAPLUS
 DOCUMENT NUMBER: 128:179454
 TITLE: Process for producing cyclodepsipeptide compounds with microorganism
 INVENTOR(S): Ohyama, Makoto; Takahashi, Masaaki; Shigematsu, Yoshiya; Sakanaka, Osamu; Murai, Yasushi; Iinuma, Katsuharu
 PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805655	A1	19980212	WO 1997-JP2772	19970807
W: AU, CA, CN, JP, KR, NO, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, NL, SE				
CA 2262679	AA	19980212	CA 1997-2262679	19970807
AU 9737844	A1	19980225	AU 1997-37844	19970807
AU 732293	B2	20010412		
EP 930304	A1	19990721	EP 1997-934736	19970807
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
CN 1230182	A	19990929	CN 1997-197905	19970807
CN 1082052	B	20020403		
NZ 334073	A	20001027	NZ 1997-334073	19970807
NO 9900520	A	19990324	NO 1999-520	19990204
US 6043058	A	20000328	US 1999-242041	19990205
KR 2000029822	A	20000525	KR 1999-700967	19990205
HK 1021977	A1	20020726	HK 2000-100871	20000214
US 6146853	A	20001114	US 2000-505294	20000216
PRIORITY APPLN. INFO.:			JP 1996-208201	A 19960807
			WO 1997-JP2772	W 19970807

AB Substance PF1022G, a novel cyclodepsipeptide represented by formula (D), is produced together with known cyclodepsipeptides, i.e., Substances PF1022F and PF1022H by culturing a bacterium which produces the Substances PF1022F, PF1022G and PF1022H, typified by the known PF1022 strain (deposited under the accession number FERM BP-2671) which is a filamentous fungus belonging to the order Agonomycetales and which is presumed to belong to the genus Xylaria or Rosellinea of the family Xylariaceae. The PF1022F-H are useful anthelmintics. Physiol. and morphol. characteristics of the microorganism and physicochem. characteristics of PF1022G were also given.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
 ACCESSION NUMBER: 2002:110114 BIOSIS
 DOCUMENT NUMBER: PREV200200110114
 TITLE: Transformant producing substance PF1022, and method for transforming microorganism belonging to the class hyphomycetes.
 AUTHOR(S): Aoyagi, K. [Inventor]; Watanabe, M. [Inventor]; Yanai, K. [Inventor]; Murakami, T. [Inventor]
 CORPORATE SOURCE: Kanagawa, Japan
 ASSIGNEE: MEIJI SEIKA KAISHA, LTD.
 PATENT INFORMATION: US 5763221 19980609

Search Results for 10/070387_20061214

SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 9, 1998) Vol. 121, No..2, pp. 1645. print.
 CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent
 LANGUAGE: English
 ENTRY DATE: Entered STN: 24 Jan 2002
 Last Updated on STN: 26 Feb 2002

L25 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
 ACCESSION NUMBER: 1997:151554 CAPLUS
 DOCUMENT NUMBER: 126:156481
 TITLE: Recombinant preparation of anthelmintic substance PF1022 using transformed hyphomycetes strain PF1022
 INVENTOR(S): Aoyagi, Kaoru; Watanabe, Manabu; Yanai, Kohji; Murakami, Takeshi
 PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
 SOURCE: PCT Int. Appl., 21 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9700944	A1	19970109	WO 1996-JP1692	19960619
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 780468	A1	19970625	EP 1996-918848	19960619
R: DE, ES, FR, GB				
US 5763221	A	19980609	US 1997-776816	19970207
PRIORITY APPLN. INFO.:			JP 1995-155973	A 19950622
			WO 1996-JP1692	W 19960619

AB A method for transforming strain PF1022, which produces a cyclic depsipeptide (substance PF1022) and belongs to Agonomycetales of the class Hyphomycetes, by using a plasmid consisting of a promoter, a terminator, a marker gene and the gene associated with the biosynthesis of PF1022. As a result, the utilization of nutrients by the transformant and its cyclic depsipeptide productivity are improved.

L25 ANSWER 4 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 1997-202796 [18] WPIDS
 DOC. NO. CPI: C1997-064928 [18]
 TITLE: New cyclic depsipeptide PF1022 derivs. are vermicides - e.g. active against Haemonchus contortus
 DERWENT CLASS: B02; B03; B04; C02
 INVENTOR: ACHIM H; BONSE G; HARDER A; IINUMA K; JESCHKE P; MATSUMOTO M; MATSUMOTO M; MENCKE N; MURAI Y; NORBERT M; OHYAMA M; OKADA U; OKADA Y; SAKANAKA O; TAKAHASHI M
 PATENT ASSIGNEE: (FARB-C) BAYER AG; (MEIJ-C) MEIJI SEIKA CO; (MEIJ-C) MEIJI SEIKA KAISHA LTD
 COUNTRY COUNT: 42

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 9711064	A1	19970327 (199718)*	JA	167[0]		
AU 9670019	A	19970409 (199731)	EN			

Search Results for 10/070387_20061214

NO 9801250	A	19980522	(199830)	NO
CZ 9800855	A3	19980812	(199839)	CS
JP 09512604	X	19981124	(199906)	JA
EP 903347	A1	19990324	(199916)	EN
CN 1201456	A	19981209	(199917)	ZH
MX 9802268	A1	19980801	(200014)	ES
BR 9610527	A	19991221	(200017)	PT
NZ 318515	A	20000526	(200033)	EN
KR 99063676	A	19990726	(200043)	KO [0]
AU 727532	B	20001214	(200103)	EN
HU 2000001164	A2	20001128	(200103)	HU
NO 310622	B1	20010730	(200151)	NQ
US 6329338	B1	20011211	(200204)	EN
IL 123776	A	20020912	(200279)	EN
MX 211809	B	20021205	(200413)	ES
CN 1082051	C	20020403	(200516)	ZH
EP 903347	B1	20050720	(200547)	EN
DE 69634961	E	20050825	(200557)	DE
CZ 295705	B6	20051012	(200571)	CS
ES 2246496	T3	20060216	(200615)	ES
DE 69634961	T2	20060420	(200628)	DE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9711064	A1	WO 1996-JP2730	19960920
AU 9670019	A	AU 1996-70019	19960920
AU 727532	B	AU 1996-70019	19960920
BR 9610527	A	BR 1996-10527	19960920
CN 1201456	A	CN 1996-198101	19960920
CN 1082051	C	CN 1996-198101	19960920
DE 69634961	E	DE 1996-634961	19960920
EP 903347	A1	EP 1996-931283	19960920
EP 903347	B1	EP 1996-931283	19960920
DE 69634961	E	EP 1996-931283	19960920
ES 2246496	T3	EP 1996-931283	19960920
IL 123776	A	IL 1996-123776	19960920
NZ 318515	A	NZ 1996-318515	19960920
NO 9801250	A	WO 1996-JP2730	19960920
CZ 9800855	A3	WO 1996-JP2730	19960920
JP 09512604	X	WO 1996-JP2730	19960920
EP 903347	A1	WO 1996-JP2730	19960920
BR 9610527	A	WO 1996-JP2730	19960920
NZ 318515	A	WO 1996-JP2730	19960920
KR 99063676	A	WO 1996-JP2730	19960920
HU 2000001164	A2	WO 1996-JP2730	19960920
NO 310622	B1	WO 1996-JP2730	19960920
US 6329338	B1	WO 1996-JP2730	19960920
MX 211809	B	WO 1996-JP2730	19960920
EP 903347	B1	WO 1996-JP2730	19960920
DE 69634961	E	WO 1996-JP2730	19960920
CZ 295705	B6	WO 1996-JP2730	19960920
JP 09512604	X	JP 1997-512604	19960920
CZ 9800855	A3	CZ 1998-855	19960920
CZ 295705	B6	CZ 1998-855	19960920
NO 9801250	A	NO 1998-1250	19980319
NO 310622	B1	NO 1998-1250	19980319
KR 99063676	A	KR 1998-702138	19980323
MX 9802268	A1	MX 1998-2268	19980323
MX 211809	B	MX 1998-2268	19980323
US 6329338	B1	US 1998-43558	19980520

Search Results for 10/070387_20061214

HU 2000001164 A2
 DE 69634961 T2
 DE 69634961 T2
 DE 69634961 T2

HU 2000-1164 19960920
 DE 1996-634961 19960920
 EP 1996-931283 19960920
 WO 1996-JP2730 19960920

FILING DETAILS:

PATENT NO	KIND	PATENT NO	
AU 727532	B	Previous Publ	AU 9670019
CZ 295705	B6	Previous Publ	CZ 9800855
DE 69634961	E	Based on	EP 903347
ES 2246496	T3	Based on	EP 903347
NO 310622	B1	Previous Publ	NO 9801250
AU 9670019	A	Based on	WO 9711064
CZ 9800855	A3	Based on	WO 9711064
JP 09512604	X	Based on	WO 9711064
EP 903347	A1	Based on	WO 9711064
BR 9610527	A	Based on	WO 9711064
NZ 318515	A	Based on	WO 9711064
KR 99063676	A	Based on	WO 9711064
HU 2000001164	A2	Based on	WO 9711064
AU 727532	B	Based on	WO 9711064
US 6329338	B1	Based on	WO 9711064
IL 123776	A	Based on	WO 9711064
EP 903347	B1	Based on	WO 9711064
DE 69634961	E	Based on	WO 9711064
CZ 295705	B6	Based on	WO 9711064
DE 69634961	T2	Based on	EP 903347
DE 69634961	T2	Based on	WO 9711064

PRIORITY APPLN. INFO: JP 1995-244051 19950922
 WO 1996-JP2730 19960920

AN 1997-202796 [18] WPIDS

AB WO 1997011064 A1 UPAB: 20060113

Cyclic depsipeptide PF1022 derivs. of formula (I) and their salts are new:

Q1 = phenyl p-substd. by R2 and Q2 = phenyl p-substd. by R1, or Q1 = R6 and Q2 = R5; R1, R2 = amino-alkO, thiocarbamoyl-alkO, cyano-alkO, protected amino-alkO, N-mono- or N,N-di(alk)amino-alkO, N,N-(di-alkOalk)amino-alkO, CycA-alkO, Het-alkO, 2-6C alkanoyl (opt. substd. by halo or OH), mono- or di-alk-carbamoyl, CycA-carbonyl, N-mono- or N,N-di-alk-amino-alkO carbonyl, CycA-amino-1-5C alkoxy carbonyl, formyl-oxy 1-5C alkylcarbonyl, COOH, t.-Bu, 2-aminothiazolyl or t.-BuO; R1 may also be H; CycA = 5-6 membered cyclic amino containing 1 or more N and opt. O and/or S; Het = 5- or 6-membered opt. unsatd. heterocycl containing 1-3 O, N and/or S and opt. substd. by alk, 3-6C cycloalkyl or phenyl (opt. substd. by Cl, Br or F); alk = 1-6C alkyl, or R1 = H or morpholino, and R2 = morpholino or Me, provided that R1 is not N when R2 = Me; R5,R6 = carboxy, protected carboxy, alkO-carbonyl, CycA (opt. benzo-fused) or Me; R6 may also be H provided that R5 is not phenyl.

USE - (I) are vermicides active against e.g. Haemonchus contortus and Nippostrongylus brasiliensis. Dosage is \geq 0.05 mg/kg orally or \geq 1 (pref. 5-10) ppm for topical use.

Member(0005)

ABEQ JP 09512604 X UPAB 20060113

Cyclic depsipeptide PF1022 derivs. of formula (I) and their salts are new:

Q1 = phenyl p-substd. by R2 and Q2 = phenyl p-substd. by R1, or Q1 = R6 and Q2 = R5; R1, R2 = amino-alkO, thiocarbamoyl-alkO, cyano-alkO, protected amino-alkO, N-mono- or N,N-di(alk)amino-alkO,

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N,N-(di-alkOalk)amino-alkO, CycA-alkO, Het-alkO, 2-6C alkanoyl (opt. subst. by halo or OH), mono- or di-alk-carbamoyl, CycA-carbonyl, N-mono- or N,N-di-alk-amino-alkO carbonyl, CycA-amino-1-5C alkoxycarbonyl, formyl-oxy 1-5C alkylcarbonyl, COOH, t.-Bu, 2-aminothiazolyl or t.-BuO; R1 may also be H; CycA = 5-6 membered cyclic amino contg. 1 or more N and opt. O and/or S; Het = 5- or 6-membered opt. unsatd. heterocyclyl contg. 1-3 O, N and/or S and opt. subst. by alk, 3-6C cycloalkyl or phenyl (opt. subst. by Cl, Br or F); alk = 1-6C alkyl, or R1 = H or morpholino, and R2 = morpholino or Me, provided that R1 is not N when R2 = Me; R5,R6 = carboxy, protected carboxy, alkO-carbonyl, CycA (opt. benzo-fused) or Me; R6 may also be H provided that R5 is not phenyl.

USE - (I) are vermicides active against e.g. Haemonchus contortus and Nippostrongylus brasiliensis. Dosage is ≥ 0.05 mg/kg orally or ≥ 1 (pref. 5-10) ppm for topical use.

Member(0006)

ABEQ EP 903347 A1 UPAB 20060113

Cyclic depsipeptide PF1022 derivs. of formula (I) and their salts are new:

Q1 = phenyl p-substd. by R2 and Q2 = phenyl p-substd. by R1, or Q1 = R6 and Q2 = R5; R1, R2 = amino-alkO, thiocarbamoyl-alkO, cyano-alkO, protected amino-alkO, N-mono- or N,N-di(alk)amino-alkO, N,N-(di-alkOalk)amino-alkO, CycA-alkO, Het-alkO, 2-6C alkanoyl (opt. subst. by halo or OH), mono- or di-alk-carbamoyl, CycA-carbonyl, N-mono- or N,N-di-alk-amino-alkO carbonyl, CycA-amino-1-5C alkoxycarbonyl, formyl-oxy 1-5C alkylcarbonyl, COOH, t.-Bu, 2-aminothiazolyl or t.-BuO; R1 may also be H; CycA = 5-6 membered cyclic amino contg. 1 or more N and opt. O and/or S; Het = 5- or 6-membered opt. unsatd. heterocyclyl contg. 1-3 O, N and/or S and opt. subst. by alk, 3-6C cycloalkyl or phenyl (opt. subst. by Cl, Br or F); alk = 1-6C alkyl, or R1 = H or morpholino, and R2 = morpholino or Me, provided that R1 is not N when R2 = Me; R5,R6 = carboxy, protected carboxy, alkO-carbonyl, CycA (opt. benzo-fused) or Me; R6 may also be H provided that R5 is not phenyl.

USE - (I) are vermicides active against e.g. Haemonchus contortus and Nippostrongylus brasiliensis. Dosage is ≥ 0.05 mg/kg orally or ≥ 1 (pref. 5-10) ppm for topical use.

L25 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:103806 BIOSIS

DOCUMENT NUMBER: PREV199698675941

TITLE: Studies on the central nervous system effects of PF1022A in rats.

AUTHOR(S): Chen, Wency [Reprint author]; Terada, Mamoru.

CORPORATE SOURCE: Dep. Parasitol., Sch. Med., Hammamatsu Univ., 3600 Handa-cho, Hammamatsu 431-31, Japan

SOURCE: Chinese Pharmaceutical Journal, (1995) Vol. 47, No. 5, pp. 437-445.

CODEN: CYHCEX. ISSN: 1016-1015.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 12 Mar 1996

Last Updated on STN: 13 Mar 1996

AB The effects of PF1022A, an antinematodal agent with a depsipeptide structure, on the central nervous system were investigated in Wistar rats. Central nervous function responses, such as sleeping time, motor activity and feeding behavior, were examined. Intraperitoneal injection of PF1022A at a dose that produces antinematodal action did not modify the steeping time induced by pentobarbital. Similar results were also observed for motor activity and food intake. However, these responses were markedly influenced by an intracerebro-ventricular (i.c.v.) injection of PF1022A into rats. Central nervous depression by i.c.v. injection of PF1022A was significantly

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different from the vehicle-treated rats. The data indicate that PF1022A does not readily penetrate the blood-brain barrier which may explain the low efficacy of this compound against worms present in the brains of hosts.

L25 ANSWER 6 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 1990-248114 [33] WPIDS
 DOC. NO. CPI: C1990-107114 [21]
 TITLE: New macrocyclic lactam-lactone derivative PF 1022 - useful as anthelmintic for human and veterinary medicine, prepared by culturing fungus FERM BP 2671
 DERWENT CLASS: B03; C02; D16
 INVENTOR: AKAI N; ARAIDA M; MIYADOH S; MIYAJI S; NIIDA M; OKADA T; SASAKI T; SEZAKI M; SHIMIZU N; SHIMIZU T; SHOMURA T; TAKAGI M; YAGUCHI T
 PATENT ASSIGNEE: (MEIJ-C) MEIJI SEIKA CO; (MEIJ-C) MEIJI SEIKA KAISHA LTD
 COUNTRY COUNT: 18

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
EP 382173	A	19900816	(199033)*	EN	20[4]	
AU 9049215	A	19900816	(199040)	EN		
NO 9000528	A	19900903	(199041)	NO		
CA 2009508	A	19900807	(199043)	EN		
JP 03035796	A	19910215	(199113)	JA		
CN 1046940	A	19901114	(199130)	ZH		
US 5116815	A	19920526	(199224)	EN	13	
NO 176766	B	19950213	(199511)	NO		
EP 382173	B1	19951206	(199602)	EN	21[4]	
DE 69023934	E	19960118	(199608)	DE		
ES 2083392	T3	19960416	(199623)	ES		
JP 2608479	B2	19970507	(199723)	JA	12[0]	
KR 132051	B1	19980411	(200010)	KO		
CA 2009508	C	20010703	(200140)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 382173 A		EP 1990-102328	19900206
JP 03035796 A		JP 1989-26739	19890207
NO 176766 B		NO 1990-528	19900205
DE 69023934 E		DE 1990-69023934	19900206
EP 382173 B1		EP 1990-102328	19900206
DE 69023934 E		EP 1990-102328	19900206
ES 2083392 T3		EP 1990-102328	19900206
JP 03035796 A		JP 1990-25176	19900206
JP 2608479 B2		JP 1990-25176	19900206
US 5116815 A		US 1990-475544	19900206
CA 2009508 C		CA 1990-2009508	19900207
KR 132051 B1		KR 1990-1460	19900207

FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 69023934 E	Based on	EP 382173 A
ES 2083392 T3	Based on	EP 382173 A
JP 2608479 B2	Previous Publ	JP 03035796 A
NO 176766 B	Previous Publ	NO 9000528 A

Search Results for 10/070387_20061214

PRIORITY APPLN. INFO: JP 1989-26739 19890207
JP 1990-25176 19900206

AN 1990-248114 [33] WPIDS

AB EP 382173 A UPAB: 20060106

The macrocyclic cpd. of formula (I), designated PF1022, is new.

(I) is produced by culturing the fungus (Agnomycetales) FERM

BP-2671. The fungus is grown under submerged aerobic conditions at 15-30
(pref. about 26) deg.C on a conventional nutrient medium. (I) present in
the cells is extracted, e.g. with aqueous acetone, while that in the culture
supernatant can be adsorbed onto Dianion HP-20, or extracted with
immiscible organic solvent. Further purifcn. is e.g. by silica gel
chromatography.

USE - (I) is an anthelmintic effective against a wide variety of
parasites, and useful in human or veterinary medicine. It is administered
orally (e.g. at 0.2-3 mg/kg) or parenterally (e.g. at 0.1-10 mg/kg), or to
prevent infestation incorporates into the feed at 5-10ppm. @ (20pp
Dwg.No.0/4)@

Member(0007)

ABEQ US 5116815 A UPAB 20060106

A new substance, PF 1022, is of formula (I), and is
characterised by MS, Sp. rotation, UV, IR, ¹H-NMR, ¹³C-NMR spectra. (I)
may be obtd. e.g. by aerobic cultivation of fungus FERM BP-2671 or
mutants, and chromatographic sepn. purifcn.

USE - Anthelmintic for humans and animals at dosage e.g.
0.01-10 (0.1-10)mg/kg p.e.

Member(0012)

ABEQ JP 2608479 B2 UPAB 20060106

The macrocyclic cpd. of formula (I), designated PF1022, is new.

(I) is produced by culturing the fungus (Agnomycetales) FERM

BP-2671. The fungus is grown under submerged aerobic conditions at 15-30
(pref. about 26) deg.C on a conventional nutrient medium. (I) present in
the cells is extracted, e.g. with aq. acetone, while that in the culture
supernatant can be adsorbed onto Dianion HP-20, or extracted with
immiscible organic solvent. Further purifcn. is e.g. by silica gel
chromatography.

USE - (I) is an anthelmintic effective against a wide variety of
parasites, and useful in human or veterinary medicine. It is administered
orally (e.g. at 0.2-3 mg/kg) or parenterally (e.g. at 0.1-10 mg/kg), or to
prevent infestation incorporates into the feed at 5-10ppm.

Search Results for 10/070387_20061214

L28 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1059375 CAPLUS
DOCUMENT NUMBER: 142:51821
TITLE: Immobilized metal ion affinity chromatography for purification of recombinant proteins fused with peptides capable of binding a metal ion
INVENTOR(S): Byrd, Devon R. N.; Esposito, Dominic; Potter, Robert Jason; Chappell, Thomas
PATENT ASSIGNEE(S): Invitrogen Corporation, USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004106361	A2	20041209	WO 2004-US16988	20040601
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006030007	A1	20060209	US 2004-857435	20040601
PRIORITY APPLN. INFO.:			US 2003-474220P	P 20030530

OTHER SOURCE(S): MARPAT 142:51821
AB The invention relates generally to affinity peptides having binding activity for metal ion affinity chromatog. media. The invention further relates to vectors which encode these affinity peptides and use of these affinity peptides for the purification of proteins of interest. The invention also relates to fusion proteins comprising affinity peptides of the invention. The sequences and formula of the affinity peptides capable of binding nickel ions are provided. The affinity peptides are removed from and/or added to the fusion proteins by intein cis or trans-splicing. The NCBI Mol. Modeling Database (MMDB) was queried with the terms "nickel", "copper", "zinc", etc. A particular query would yield structural data for a particular set of proteins. Binding of peptides to nickel matrixes was predicted from the structural data.

L28 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:527718 CAPLUS
DOCUMENT NUMBER: 141:242096
TITLE: Para-position derivatives of fungal antihelmintic cyclodepsipeptides engineered with Streptomyces venezuelae antibiotic biosynthetic genes
AUTHOR(S): Yanai, Koji; Sumida, Naomi; Okakura, Kaoru; Moriya, Tatsuki; Watanabe, Manabu; Murakami, Takeshi
CORPORATE SOURCE: Microbiological Resources and Technology Laboratories, Meiji Seika Kaisha, Ltd., Odawara-shi, Kanagawa, 250-0852, Japan
SOURCE: Nature Biotechnology (2004), 22(7), 848-855
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

Search Results for 10/070387_20061214

AB PF1022A, a cyclooctadepsipeptide possessing strong anthelmintic properties and produced by the filamentous fungus *Rosellinia* sp. PF1022, consists of four alternating residues of N-methyl-L-leucine and four residues of D-lactate or D-phenyllactate. PF1022A derivs. obtained through modification of their benzene ring at the para-position with nitro or amino groups act as valuable starting materials for the synthesis of compds. with improved anthelmintic activities. Here we describe the production of such derivs. by fermentation

through

metabolic engineering of the PF1022A biosynthetic pathway in *Rosellinia* sp. PF1022. Three genes cloned from *Streptomyces venezuelae*, and required for the biosynthesis of p-aminophenylpyruvate from chorismate in the chloramphenicol biosynthetic pathway, were expressed in a chorismate mutase-deficient strain derived from *Rosellinia* sp. PF1022. Liquid chromatog.-mass spectrometry and NMR analyses confirmed that this approach facilitated the production of PF1022A derivs. specifically modified at the para-position. This fermentation method is

environmentally safe and can be used for the industrial scale production of PF1022A derivs.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 8 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003108360 EMBASE

TITLE: Effects of KHEYLRFamide and KNEFIRFamide on cyclic adenosine monophosphate levels in *Ascaris suum* somatic muscle.

AUTHOR: Thompson D.P.; Davis J.P.; Larsen M.J.; Coscarelli E.M.; Zinser E.W.; Bowman J.W.; Alexander-Bowman S.J.; Marks N.J.; Geary T.G.

CORPORATE SOURCE: D.P. Thompson, Pharmacia Animal Health, 7000 Portage Road, Kalamazoo, MI 49001-0199, United States.

SOURCE: david.p.thompson@pharmacia.com International Journal for Parasitology, (2003) Vol. 33, No. 2, pp. 199-208.

Refs: 44

ISSN: 0020-7519 CODEN: IJPYBT

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

030 Pharmacology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 27 Mar 2003

Last Updated on STN: 27 Mar 2003

AB KHEYLRF-NH(2) (AF2) is a FMRFamide-related peptide (FaRP) present in parasitic and free-living nematodes. At concentrations as low as 10 pM, AF2 induces a biphasic tension response, consisting of a transient relaxation followed by profound excitation, in neuromuscular strips prepared from *Ascaris suum*. In the present study, the effects of AF2 on cyclic adenosine monophosphate (cAMP), cyclic guanosine monophosphate (cGMP) and inositol-1,4,5-triphosphate (IP(3)) levels were measured following muscle tension recordings from 2 cm neuromuscular strips prepared from adult *A. suum*. AF2 induced a concentration- and time-dependent increase in cAMP, beginning at 1 nM; cAMP levels increased by 84-fold following 1 h exposure to 1 μM AF2. cGMP and IP(3) levels were unaffected by AF2 at concentrations ≤ 1 μM. AF2-induced stimulation of cAMP was unaffected by removal of the dorsal-or ventral nerve cord, even though this form of denervation abolished the excitatory

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phase of the tension response. The effects of 0.1 and 1 μM AF2 on cAMP were also unaffected by 10 μM SDPNFLRF-NH(2) (PF1, an inhibitory FaRP) and 10 μM PF1022A (an inhibitory cyclodepsipeptide), even though each of these peptides abolished the excitatory phase of the tension response induced by AF2. Within an alanine-scan series of AF2 analogues, only KHAYLRF-NH(2) stimulated cAMP production with equipotency to AF2; the effects of this peptide on muscle tension also mimicked AF2. Another excitatory FaRP present in nematodes, KNEFIRF-NH(2) (AF1), also stimulated cAMP production, but was 100-fold less potent than AF2. The stimulatory effects of AF1 on tension and cAMP levels were blocked by an alanine-substituted analogue of this peptide (Ala(6)-AF1, KNEFIWF-NH(2)), while the stimulatory effects of AF2 on tension and cAMP were not affected by this analogue. AF2 and AF1 increase *A. suum* somatic muscle cAMP by targeting different receptors. Increases in cAMP stimulated by AF2 can be decoupled from the excitatory response caused by this peptide, and it is not possible to establish a causal linkage between the contractile response elicited by this peptide and its effects on cAMP accumulation.

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L28 ANSWER 4 OF 8 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2002-292270 [33] WPIDS
 DOC. NO. CPI: C2002-085925 [33]
 TITLE: Use of calcium transmembrane receptors for screening and identifying anthelmintic and arthropodicidal agents for medicine or agriculture
 DERWENT CLASS: B04; C07; D16; P14
 INVENTOR: HARDER A; SAEGER B; SAMSON-HIMMELSTJERNA G V;
 SCHMITT-WREDE H; SCHMITT-WREDE H P; VON
 SAMSON-HIMMELSTJERNA G; WUNDERLICH F
 PATENT ASSIGNEE: (FARB-C) BAYER AG; (HARD-I) HARDER A; (SAEG-I) SAEGER B;
 (SAMS-I) SAMSON-HIMMELSTJERNA G V; (SCHM-I) SCHMITT-WREDE
 H; (WUND-I) WUNDERLICH F
 COUNTRY COUNT: 96

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002020830	A2	20020314	(200233)*	DE	128 [15]	
DE 10053785	A1	20020328	(200233)	DE		
AU 2001093789	A	20020322	(200251)	EN		
EP 1317562	A2	20030611	(200339)	DE		
JP 2004508052	W	20040318	(200420)	JA	201	
CN 1543508	A	20041103	(200514)	ZH		
US 20050037436	A1	20050217	(200514)	EN		
NZ 524533	A	20050429	(200532)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002020830	A2	WO 2001-EP9771	20010824
DE 10053785	A1	DE 2000-10053785	20001030
AU 2001093789	A	AU 2001-93789	20010824
CN 1543508	A	CN 2001-818524	20010824
EP 1317562	A2	EP 2001-974211	20010824
NZ 524533	A	NZ 2001-524533	20010824
EP 1317562	A2	WO 2001-EP9771	20010824
JP 2004508052	W	WO 2001-EP9771	20010824
US 20050037436	A1	WO 2001-EP9771	20010824
NZ 524533	A	WO 2001-EP9771	20010824

Search Results for 10/070387_20061214

JP 2004508052 W
US 20050037436 A1

JP 2002-525836 20010824
US 2003-363946 20030725

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001093789 A	Based on	WO 2002020830 A
EP 1317562 A2	Based on	WO 2002020830 A
JP 2004508052 W	Based on	WO 2002020830 A
NZ 524533 A	Based on	WO 2002020830 A

PRIORITY APPLN. INFO: DE 2000-10053785 20001030
DE 2000-10044098 20000907
DE 2000-10044089 20000907

AN 2002-292270 [33] WPIDS
AB WO 2002020830 A2 UPAB: 20060119

NOVELTY - Use of calcium channel transmembrane receptors (A) from helminths or arthropods for identifying anthelmintic or arthropodicidal agents (B) respectively, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) use of alpha-latrotoxin (I) as agonist of helminth (A) and for identifying nematocidal/arthropodicidal agents;

(b) producing the HC110-R receptor of *Haemonchus contortus*, or homologous proteins, by expressing it, or its fragments, in prokaryotic or eukaryotic systems;

(c) host cells that can express HC110-R, or its homologs, transiently or stably;

(d) vectors for preparing cells of (c);

(e) identifying (ant)agonists of (A) or agents that alter expression of (A);

(f) compounds identified by method (e);

(g) transgenic invertebrates that contain HC110-R, or homologous proteins;

(h) determining helminth DNA using oligonucleotides that hybridize to sequences encoding HC110-R; and

(i) diagnostic kit containing a DNA sequence (or fragment) that encodes HC110-R, or homologous sequences.

ACTIVITY - Nematocide; acaricide; insecticide. No supporting data is given.

MECHANISM OF ACTION - Calcium channel (ant)agonist; vaccine.

USE - (A) are used to identify calcium channel (ant)agonists, particularly blockers that are active on receptors that bind alpha-latrotoxin (I), or agents that alter expression of (A). The identified compounds, and (I), are potentially useful for control of helminths and arthropods, particularly as nematocides, acaricides and insecticides, for use in human or veterinary medicine, agriculture, protection of stored goods and hygienic applications. DNA that encodes the preferred (A), i.e. HC110-R of *Haemonchus contortus*, or its homologs, is used to produce transgenic invertebrates (useful as test systems) and oligonucleotides from this DNA are useful for detecting DNA of helminth origin. The HC110-R protein (or its fragments or homologs) can be used in vaccines.

L28 ANSWER 5 OF 8 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2001273282 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11344131

TITLE: Latrophilin-like receptor from the parasitic nematode *Haemonchus contortus* as target for the anthelmintic depsipeptide PF1022A.

AUTHOR: Saeger B; Schmitt-Wrede H P; Dehnhardt M; Benten W P;

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Krucken J; Harder A; Von Samson-Himmelstjerna G; Wiegand H;
 Wunderlich F
CORPORATE SOURCE: Division of Molecular Parasitology and Center for
 Biological and Medical Research, Heinrich-Heine-University,
 40225 Dusseldorf, Germany.
SOURCE: The FASEB journal : official publication of the Federation
 of American Societies for Experimental Biology, (2001 May)
 Vol. 15, No. 7, pp. 1332-4.
 Journal code: 8804484. ISSN: 0892-6638.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ272270
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 18 Jun 2001
 Last Updated on STN: 2 Jan 2003
 Entered Medline: 14 Jun 2001

L28 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:239286 CAPLUS
DOCUMENT NUMBER: 128:304807
TITLE: Nematicical depsipeptide-binding nematode proteins and
 DNA sequences coding therefor and their use in
 identifying nematicides
INVENTOR(S): Harder, Achim; Scherkenbeck, Jurgen; Jeschke, Peter;
 Wunderlich, Frank; Schmitt-Wrede, Hans-Peter; Saeger,
 Beate
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany; Harder, Achim;
 Scherkenbeck, Jurgen; Jeschke, Peter; Wunderlich,
 Frank; Schmitt-Wrede, Hans-Peter; Saeger, Beate
SOURCE: PCT Int. Appl., 61 pp.
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815625	A1	19980416	WO 1997-EP5314	19970929
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19704024	A1	19980416	DE 1997-19704024	19970204
AU 9746249	A1	19980505	AU 1997-46249	19970929
PRIORITY APPLN. INFO.:			DE 1996-19641690	A 19961010
			DE 1997-19704024	A 19970204
			WO 1997-EP5314	W 19970929

AB The present invention relates to proteins which react with substances
 active against nematode parasites, i.e., from the group of cyclic or
 open-chain depsipeptides consisting of amino acids and hydroxycarboxylic
 acids. The disclosure also comprises DNA sequences encoding these
 proteins as well as the use of said proteins for identifying substances
 acting against nematode parasites. Antibodies to the nematicidal
 depsipeptides and a method for preparing these antibodies are also
 disclosed. Conjugates of keyhole limpet hemocyanin and bovine serum

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albumin with PF 1022A were prepared and used to raise anti-PF 1022A antiserum in rabbits. These antibodies were used to screen an *Haemonchus contortus* cDNA library expressed in *E. coli* to identify PF 1022A-binding proteins. The cDNAs for a 207- and a 986-amino acid protein were thus identified and sequenced.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999088869 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9871703
TITLE: PF1022A--a novel anthelmintic cyclooctadepsipeptide. Modification and exchange of the N-methyl leucine residues.
AUTHOR: Scherkenbeck J; Harder A; Plant A; Dyker H
CORPORATE SOURCE: Bayer AG, Leverkusen, Germany. JUERGEN. SCHERKENBECK.JS@bayer-ag.de
SOURCE: Bioorganic & medicinal chemistry letters, (1998 May 5) Vol. 8, No. 9, pp. 1035-40.
Journal code: 9107377. ISSN: 0960-894X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 9 Feb 1999
Last Updated on STN: 9 Feb 1999
Entered Medline: 25 Jan 1999

AB The first structure-activity relationships of the anthelmintic cyclooctadepsipeptide PF1022A have been established via a systematic exchange of the leucine residues by a series of related N-alkylated amino acids. The data presented strongly suggest that (L)-N-methyl-leucine is crucial for high in vivo activity.

L28 ANSWER 8 OF 8 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 96422584 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8825201
TITLE: Characterization of subtypes of gamma-aminobutyric acid receptors in an *Ascaris* muscle preparation by binding assay and binding of PF1022A, a new anthelmintic, on the receptors.
AUTHOR: Chen W; Terada M; Cheng J T
CORPORATE SOURCE: Department of Parasitology, Hammamatsu University School of Medicine, Japan.
SOURCE: Parasitology research, (1996) Vol. 82, No. 2, pp. 97-101.
Journal code: 8703571. ISSN: 0932-0113.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
Entered Medline: 5 Dec 1996

AB We examined the effect of PF1022A, one of the gabergic anthelmintics newly developed in Japan, on gamma-aminobutyric acid (GABA) receptors using a radioligand binding technique in isolated membrane preparations of the nematode *Ascaris suum*. Membrane protein was prepared from the homogenate of somatic muscle cells after ultracentrifugation. In addition to the basic binding of [^{2,3}-³H-(N)]-GABA, the radioligand [methyl-³H]-picuculline is used to identify the GABAA receptor, whereas [butyl-4-³H]-baclofen is employed for

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GABAB receptor sites. The dissociation constants (K_d values) and the maximal numbers of binding sites (B_{max} values) from Scatchard plotting for GABA receptors are close to those obtained in mammalian brain. PF1022A displaced in a concentration-dependent way the binding of [$2,3\text{-}^3\text{H(N)}$] -GABA and [$\text{methyl-}^3\text{H}$] -bicuculline as did other specific gabergic agents. In addition, PF1022A decreased the binding of [$\text{butyl-}^4\text{H}$] -baclofen at a higher concentration, although this binding did not represent GABAB sites. In a comparison of the inhibition constants (K_i values) of PF1022A with those of other agents, it is conclusive that PF1022A bound with GABA receptors. A direct effect of PF1022A on GABA receptors can thus be postulated.